87-1804

No.

In The

Supreme Court of the United States

October Term, 1987

TRI-BIO LABORATORIES, INC.,

Petitioner,

vs.

THE UNITED STATES OF AMERICA AND FOOD AND DRUG ADMINISTRATION,

Respondents.

PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT

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QUESTIONS PRESENTED

The Food, Drug and Cosmetic Act, 21 U.S.C. § 301 *et seq.* (the "Act"), required the manufacturer of a new animal drug to submit a New Animal Drug Applicaton ("NADA") to the Food and Drug Administration ("FDA") for approval of the safety and effectiveness of the drug before it is marketed.

The questions presented are:

1. Whether the Act requires the manufacturer of a generic animal drug which is identical in both active and inactive ingredients and is bioequivalent to a pioneer animal drug previously approved by the FDA as safe and effective must reprove to the FDA that the generic drug is safe and effective by duplicative testing which involves substantial financial expense and the needless destruction of laboratory animals?

2. Whether the Act authorizes the FDA to promulgate a regulation for the sole purpose of protecting an alleged proprietary interest of a pioneer drug applicant?

3. Whether the owner of a pioneer drug has a "reasonable investment-backed expectation" such as to prohibit the FDA from relying on the pioneer's data concerning safety and effectiveness in considering a NADA of a generic manufacturer?

LIST OF PARTIES

The caption of the case contains the names of all parties to the proceedings in the courts below whose judgment is sought to be reviewed.

RULE 28.1 LIST

Petitioner, Tri-Bio Laboratories, Inc., has no parent companies, subsidiaries, or corporate affiliates, except as follows:

Tri-Bio Laboratories owns a controlling interest in Magna Technologies, Inc., a North Carolina business corporation engaged in the manufacture and sale of chemical products in the veterinary industry.

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No.

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THE UNITED STATES OF AMERICA AND FOOD AND DRUG ADMINISTRATION,

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PETITION FOR WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT

The petitioner, Tri-Bio Laboratories, Inc., respectfully prays that a writ of certiorari issue to review the judgment and opinion of the United States Court of Appeals for the Third Circuit, entered in the above-entitled proceeding on December 29, 1987.

OPINIONS BELOW

The opinion of the Court of Appeals for the Third Circuit

is reported at 836 F.2d 135, and is reprinted in the appendix hereto, p. 5a, *infra*.

The memorandum judgment order of the United States District Court for the Middle District of Pennsylvania (Muir, D.J.) has not been reported. It is reprinted in the appendix hereto, p. 26a, *infra*. The Report of Magistrate, adopted by the district court, is not reported and is reprinted in the appendix hereto, p. 30a, *infra*.

JURISDICTION

Subject matter jurisdiction for the complaint was invoked pursuant to federal question jurisdiction under 28 U.S.C. § 1331 to have the Middle District Court of Pennsylvania properly interpret 21 U.S.C. §§ 321(w) and 360b. 28 U.S.C. § 1337 was also invoked as this is a civil action arising under an Act of Congress regulating commerce. Additionally, 28 U.S.C. § 1346(a)(2) was invoked in that this is a civil action against the United States founded upon the Constitution, an Act of Congress, or a regulation of an executive department, in the event a basis for recovery of damages would arise during the course of the proceedings. Finally, the complaint sought judicial review of a final agency action based in part on 5 U.S.C. § 551 *et seq.* and § 701 *et seq.* (the Administrative Procedure Act).

On January 27, 1987, the Middle District granted the respondents' motion for summary judgment and dismissed the complaint.

Appellate jurisdiction before the Court of Appeals for the Third Circuit was invoked pursuant to 28 U.S.C. § 1291 as an appeal from the final order of the Middle District. The United States Court of Appeals for the Third Circuit by opinion and order of December 29, 1987, affirmed the order of the United

States District Court for the Middle District of Pennsylvania.

Thereafter, Tri-Bio Laboratories, Inc., timely filed its petition for rehearing on January 15, 1988, pursuant to an extension of time granted by the Court of Appeals by order of January 12, 1988. By order of February 1, 1988, the Court of Appeals denied petitioner's petition for rehearing.

Jurisdiction of this Court to review the judgment of the United States Court of Appeals for the Third Circuit is invoked under 28 U.S.C.A. § 1254(1).

STATUTES AND REGULATIONS INVOLVED

21 U.S.C. § 321(w) (set forth in appendix, p. 85a).

21 U.S.C. § 360b (set forth in appendix, p. 64a).

21 C.F.R. § 514.1(a) (1987) originally codified at 21 C.F.R. § 135.4a(a), redesignated to 21 C.F.R. § 514.1(a) by 40 Fed. Reg. 1380-2, 13825 (1975) (set forth in appendix, p. 86a).

STATEMENT OF THE CASE

The dispute between Tri-Bio Laboratories, Inc., ("Tri-Bio") and the Food and Drug Administration ("FDA") has its origins in the FDA's denial of a New Animal Drug Application ("NADA") Tri-Bio submitted for Gentaject in August, 1981. Gentaject is an injectable drug recommended by its labeling for use in the treatment of one-day old chicks to prevent early mortality caused by certain gram negative bacteria. It is an exact duplicate in both active and inactive ingredients of a drug product sold under the trade name "Garasol" manufactured by Schering Corporation for identical indications, which product was approved by the FDA as both safe and effective in 1978. The sole active

ingredient in both Garasol and Gentaject is gentamiacin sulfate, a drug originally patented by Schering in May of 1963, which patent expired in May of 1980.

In its NADA seeking the premarketing approval of Gentaject, Tri-Bio sought to incorporate the FDA's prior determination of the safety and efficacy of Garasol, as being supportive of the safety and efficacy of Gentaject (A208). The FDA denied this request, indicating that it would not permit TriBio's NADA to rely on any information in the previously approved duplicate's NADA, nor on the FDA's own prior determination that the duplicate composition was, in fact, safe and effective.

In response to the FDA's position and faced with an enforcement action initiated by the FDA, Tri-Bio filed a complaint for relief in the form of a declaratory judgment in the United States District Court for the Middle District of Pennsylvania, on April 29, 1983, seeking a declaration from the district court that Gentaject was not a "new animal drug" subject to the FDA premarketing NADA approval process (A269-272). During the course of that litigation, a Statement of Undisputed Facts (A273-280) was executed by the parties wherein the FDA admitted that Gentaject is identical in all respects to Garasol, which was previously approved by the FDA as being a safe and effective animal drug when used in accordance with its labelling. Additionally, the FDA admitted that Gentaject is similarly safe and effective for such use. Notwithstanding these admissions, the FDA continued in its assertion that Gentaject could not be marketed until Tri-Bio proved through duplicative tests what the FDA had admitted.

This initial litigation was voluntarily dismissed by the parties, *without prejudice*, prior to trial of the issue of the drug's non-new animal drug status before the district court. By stipulation of voluntary dismissal filed July 3, 1984 (A281-282), Tri-Bio agreed

to submit to the FDA a "Citizen's Petition" seeking an administrative declaration that Gentaject is not a new animal drug within the meaning of 21 U.S.C § 321(w). *See* 21 C.F.R. § 10.30. In return, the FDA agreed not to initiate enforcement proceedings against Tri-Bio, its officers, or Gentaject, by virtue of the claimed new drug status of Gentaject, for a period of at least 18 months. Finally, the stipulation provided that all admissions set forth in the various pleadings filed in the litigation would apply to any subsequent litigation between the parties.

In accordance with the stipulation, Tri-Bio filed its Citizen's Petition with the FDA on September 13, 1984. In the petition, Tri-Bio requested the agency declare "Gentaject" not to be a new animal drug as that term is defined in § 321(w) of the Act or alternatively to permit Tri-Bio's NADA to rely on the safety and effectiveness data already in the FDA's knowledge obtained from the NADA submitted by Schering Corporation in the filing of its NADA for Garasol. By letter dated December 17, 1985, Tri-Bio's petition was denied (A146-160). The commissioner concluded that Gentaject was a "new animal drug", and could not be marketed without prior FDA approval of an NADA containing full safety and effectiveness data. Thereafter, Tri-Bio filed the instant lawsuit on January 21, 1986.

The undisputed facts presented to the district court established that Gentaject and Garasol are recommended by their labeling for the same purposes, are identical in every respect, and are equally safe and effective for their labeled indications. Additionally, the FDA failed to deny Tri-Bio's contention that it is scientifically unnecessary to re-establish the safety and effectiveness of a drug that is already known to be safe and effective. In response to motion for summary judgment filed by the FDA, and in support of its own cross-motion for summary judgment, Tri-Bio offered the affidavit of an expert witness who estimated that approximately 102,580 animals would be consumed

in research to re-establish the safety and effectiveness of Gentaject. The cost of the research was estimated to be $450,000 (A187).

The district court, by memorandum judgment order of January 27, 1987, granted the FDA's motion for summary judgment and denied Tri-Bio's cross-motion. Acting on a magistrate's recommendation, the district court concluded that the FDA properly interpreted its statutory authority in formulating its policy of rejecting applications which referenced data submitted by previous applicants. The court further held the FDA had not acted in an arbitrary or capricious manner, nor was its decision unwarranted by the facts. Tri-Bio, on February 12, 1987, filed its notice of appeal to the Court of Appeals for the Third Circuit seeking to have the Court of Appeals reverse the grant of FDA's motion for summary judgment.

The Court of Appeals affirmed, but on different grounds than stated in the district court decision. Specifically, the Court of Appeals held that an FDA regulation which was promulgated to protect the proprietary interests of the pioneer drug manufacturer gave rise to a reasonable investment-backed expectation of agency non-use of submitted data. The Court of Appeals, assuming the regulation to be within the FDA's legitimate rulemaking authority, concluded that use of data submitted following promulgation of the regulation would constitute a Fifth Amendment "taking" requiring governmental payment of compensation which was not contemplated by the underlying statute which was silent on the issue. Reasoning further, the court held that the lack of an express statutory compensatory intent for agency use of data, supported the conclusion that the FDA regulation was properly promulgated. A timely-filed petition for rehearing was denied by order of February 1, 1988.

REASONS FOR GRANTING THE WRIT

This case involves an important question, similar to, but more compelling than the important question left open by this Court in *United States v. Generix Drug Corp.*, 460 U. S. 453 (1983). There, this Court held that a generic drug is a "new drug" for purposes of the Act until the product (and not merely its active ingredients) is generally recognized as safe and effective within the meaning of Section 201(p) of the Act. The Court left open "the issue of whether two demonstrably bioequivalent products, containing the same active ingredients but different excipients, might under some circumstances be the same 'drug'. " *id.* at 461.

Here, the FDA determined that because neither the pioneer drug, which had been approved as safe and effective and has been on the market since 1978, nor the generic drug are generally recognized as safe and effective, the generic drug is a "new drug" for all purposes of the Act, even though it is an exact duplicate and bioequivalent to the drug which the FDA has already approved. Having concluded that the generic drug is a "new drug", the FDA insists that its manufacturer prove to the FDA what the FDA admits it already knows — that the drug is safe and effective — solely to protect the proprietary interest of the pioneer applicant.

Despite conceding the "curiousness" of the result, the Court of Appeals for the Third Circuit nevertheless upheld the position of the FDA which requires generic animal drug manufacturers to needlessly kill hundreds of thousands of animals at great expense in order to demonstrate to the FDA that a generic drug product is as equally safe and effective as a previously approved and admittedly identical drug of another manufacturer. The decision approves the FDA's extension of congressionally unsanctioned patent-like protection to pioneer drug manufacturers beyond normal patent terms, in an effort to protect these manufacturers'

economic position in the marketplace from their competitors.

In addition to legitimate concerns over the needless slaughter of laboratory animals, the decision is certain to affect every citizen of the United States in that the substantial expense of reproving an animal drug's undisputed safety and efficacy acts as a bar to inexpensive generic animal drug development while maintaining an FDA-sanctioned pioneer manufacturer's monopoly that stifles competition and can only result in higher consumer prices for meat and meat products.

The Court of Appeal's holding is based solely on a 1971 regulation promulgated by the FDA which effectively prohibits the FDA from internal use of the data. The pertinent section of the regulation states:

> "Any reference to information furnished by a person other than the applicant may not be considered unless its use is authorized in a written statement signed by the person who submitted it." 21 C.F.R. Section 514.1(a) (1987) [originally codified at 21 C.F.R. Section 135.4a(a), redesignated to 21 C.F.R. Section 514.1(a) by 40 Fed. Reg. 1380-2, 13825 (1975)].

The Court of Appeals reasoned that this regulation provides the original data submitter with a reasonable investment-backed expectation that its data would not be used in considering the NADA of a competitor seeking marketing approval of an identical drug. Consequently, such internal use would be a "taking" of property without just compensation in violation of the Fifth Amendment, which was not expressly envisioned by the underlying statute. The Court of Appeals assumed the regulation to have been within the FDA's legitimate rulemaking authority, although stating that the factor was not determinative. Rather, the Court

of Appeals broadly construed this Court's decision in *Ruckelshaus v. Monsanto,* 467 U.S. 986 at 1013, n. 17 (1984) and held that the relevant consideration was the nature of the expectations of the submitter at the time the data were submitted, and held this expectation of non-use could be supplied by a "provision of law" in the form of a regulation.

The Court of Appeals' analysis assumes that the pioneer submitted its NADA in reliance on the 1971 regulation. That is, it assumes that the pioneer manufacturer would not or may not have filed its NADA in the absence of the regulation. This is a very large assumption, indeed. A safer assumption might be that the pioneer would have submitted its NADA in the absence of the regulation, or even in the face of a regulation authorizing internal FDA use of that data[1], since it is only through FDA approval of the NADA that Schering could market the product and create real value in the data.

In so ruling, the Court of Appeals departed both from its own precedents and that of this Court as espoused in *Ruckelshaus v. Monsanto,* 467 U.S. 986 (1984) and *Thomas v. Union Carbide Agricultural Products Co.,* 105 S. Ct. 3325 (1985). Never before has this Court nor the Court of Appeals for the Third Circuit held that a administrative regulation not expressly authorized by statute can form the basis for a reasonable investment-backed expectation that would give rise to a Fifth Amendment taking requiring government compensation.

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1. Curiously, the FDA does have regulations which authorize public disclosure and internal use of food color and additive registration. *See* 21 C.F.R. §§ 71.15, 171.1(h). The statutory language with regard to the food color and food additives is very similar to that with respect to the NADA process. *Compare* 21 U.S.C. § 348 and 376 with 21 U.S.C. § 360b. There is no apparent reason for the conflicting policies nor is there any reason to assume that this regulation discourages manufacturers of food additives from submitting applications, since they also have no alternative.

The regulation in question prohibits the FDA from referring to "information furnished by a person other than the applicant unless its use is authorized . . . by the person who submitted it. 21 C.F.R. § 514.1. This regulation is in direct conflict with the applicable statute. Subparagraph d(1) of 21 U.S.C. § 360b mandates that the Commissioner of the FDA shall determine an application, *e.g.*,

> "upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug . . .
>
> . . .based upon a fair evaluation of all material facts . . ."

Thus, the statute expressly contemplates agency use of previously submitted data in evaluating applications by others with respect to the same drug.

Further, the essential principle that can be derived from *Monsanto,* which the Court of Appeals rejected is that in the absence of an express statutory provision of law *prohibiting* agency non-use, the agency can use the data and the submitter cannot obtain a reasonable expectation of non-use requiring compensation. *Monsanto, supra* at 1013. The Court of Appeals dismissed this principle, by concluding that the agency can itself provide the prohibition the statute does not by means of a regulation.

The Court of Appeals' ruling in the instant case squarely conflicts with this Court's stated understanding of the Food, Drug and Cosmetic Act, by holding that the regulation provides such an expectation even without legislative support for the regulation's promulgation. Justice O'Connor, in writing the opinion of the

Court in *Thomas v. Union Carbide Agricultural Products Co., supra* at 3335, noted the Court's view that both Congress and the FDA have intended and interpreted similar related provisions of the Food, Drug and Cosmetic Act as providing no reasonable expectation of agency non-use of the data submitted:

> "[R]egistrants who submit data with notice of the scheme established by the 1978 amendments, and its qualified protection of trade secrets as defined in Section 10, can claim no property interest under state law in data subject to Section 3(c)(1)(b)(ii), *Ruckelshaus v. Monsanto Co., supra,* at ____, 104 S.Ct., at ____. Cf. 21 U.S.C. Sections 348(a)(2), 376(a)(1); 21 CFR Section 71.15 (1985), 21 CFR Section 171.1(h) (1984) (data submitted under Food and Drug Act is in public domain and follow-on registrants need not submit independent data)".

Justice Steven's opinion concurring in the judgment, likewise references his view that there is no basis for prohibiting use of submitted data even where a statute conditioning such use on an offer of payment of compensation to the original data submitter would be stricken as unconstitutional. *Thomas v. Union Carbide Agricultural Products Co., supra* at 3345-46.

The Third Circuit Court of Appeals' decision is in conflict with a decision of the Sixth Circuit Court of Appeals. In *Upjohn Mfg. Co. v. Schweiker,* 681 F.2d 480 (6th Cir. 1982) a decision upholding the FDA's approval of an abbreviated new human drug application, the Sixth Circuit stated that the new drug approval sections were not intended to provide the pioneer with patent-like protection. *Id.* at 484.

Subsequent legislative history also establishes that the FDA regulation is contrary to congressional intent and that the Court

of Appeals misconstrued *Monsanto* in holding that a reasonable expectation of non-use of submitted data may arise from a mere regulation. On September 24, 1984, Congress revised the law relating to human drugs by enacting the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. 68-417, amending Section 505, 21 U.S.C. § 355 (the "DPC-PTR Act"). In the new law, Congress expressly overruled "longstanding" FDA policy/interpretations and specifically decreed that all manufacturers of generic copies of approved pioneer human drug products (with certain exceptions) may file abbreviated NDA's which rely on specific items of information contained in the pioneer application.

In the applicable legislative history set forth in *1984 U.S. Cong. and Admin. News*, p. 2647, *et seq.*,Congress explained the reasons for the enactment of the DPC-PTR Act. In 1970 the FDA had formally adopted an abreviated new drug application procedure to enable the approval of generic human drug products that had been first approved prior to October 10, 1962, the date of enactment of the Act. *See* 35 Fed. Reg. 6574 (1970). Under this procedure, generic copies of pioneer drugs approved prior to October 10, 1962 could rely on safety and effectiveness data submitted by the pioneer. However, no drug approved for use after October 10, 1962 was entitled to use the abbreviated application procedure. The FDA has afforded similar treatment to animal drugs.

Congress explained that the need for congressional action arose from the FDA's failure to act to promulgate regulations establishing a specific procedure for reliance on data submitted by pioneer drug manufacturer's. *Id.* at 2647-49. This legislative history clearly establishes that Congress does not approve of the FDA's pre- and post-1962 distinction with respect to human drugs. It states, in substance, that the 1984 amendments were made necessary because of the FDA's erroneous interpretations of the

Act and its failure to act to correct its error. The same reasoning is equally applicable to the parallel new animal drug approval provisions. The statutory language, legislative history of the related new (human) drug application provisions, and the FDA's own inconsistent treatment of pre- and post-1962 NADA's confirms that the FDA and the Court of Appeals are frustrating congressional policy in this field.

Even assuming a "taking" would occur if the FDA were to consider a competitor's data in approving an applicant's NADA, the Court of Appeals erred in supporting the validity of the regulation by concluding Congress did not intend to compensate the pioneer applicant because the FDA Act is silent on the matter (18a). Again, the Court of Appeal's reasoning and conclusion was expressly rejected by the Supreme Court in *Monsanto*, 467 U.S. at 1017-19:

> "In determining whether a Tucker Act remedy is available for claims arising out of a taking pursuant to a federal statute, the proper inquiry is not whether the statute 'expresses an affirmative showing of congressional intent to permit recourse to a Tucker Act remedy,' but whether Congress has in the [statute] *withdrawn* the Tucker Act grant of jurisdiction to the Court of Claims to hear a suit involving the [statute] 'founded . . . upon the Constitution.' *Regional Rail Reorganization Act Cases,* 419 U.S. 102, 126, 95 S.Ct. 335, 350, 42 L.Ed.2d 320 (1974) (emphasis in original).
>
> . . . Congress' failure specifically to mention or provide for recourse against the Government may reflect a congressional belief that use of data by EPA in the ways authorized by FIFRA effects no Fifth Amendment taking or it may reflect

> Congress' assumption that the general grant of jurisdiction under the Tucker Act would provide the necessary remedy for any taking that may occur. In any event, the failure cannot be construed to reflect an unambiguous intention to withdraw the Tucker Act remedy. '[W]hether or not the United States so intended,' any taking claim under FIFRA is one 'founded . . . upon the Constitution,' and is thus remediable under the Tucker Act. *Regional Rail Reorganization Act Cases,* 419 U.S. at 126, 95 S.Ct. at 350. Therefore, where the operation of the data-consideration and data-disclosure provisions of FIFRA effect a taking of property belonging to Monsanto, an adequate remedy for the taking exists under the Tucker Act. The District Court erred in enjoining the taking."

Thus, the Tucker Act does provide a remedy even if the FDA's use of the pioneer's data is considered a taking within the meaning of the Fifth Amendment.

CONCLUSION

For the reasons stated, this petition for certiorari should be granted.

Respectfully submitted,

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APPENDIX A — ORDER OF THE UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT SUR PETITION FOR REHEARING

UNITED STATES COURT OF APPEALS
FOR THE THIRD CIRCUIT

No. 87-5123

TRI-BIO LABORATORIES, INC.,

Appellant

v.

UNITED STATES OF AMERICA and FOOD AND DRUG ADMINISTRATION,

Appellees

(D.C. Civil No. 86-0083)

SUR PETITION FOR REHEARING

Present: GIBBONS, *Chief Judge*, SEITZ, WEIS, HIGGINBOTHAM, SLOVITER, BECKER, STAPLETON, MANSMANN, GREENBERG, SCIRICA, HUTCHINSON, COWEN *Circuit Judges* and KELLY, *District Judge.**

The petition for rehearing filed by appellant in the above entitled case having been submitted to the judges who participated

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* The Honorable James McGirr Kelly, United States District Judge for the Eastern District of Pennsylvania, who sat by designation is entitled to vote for panel rehearing only.

in the decision of this court and to all the other available circuit judges of the circuit in regular active service, and no judge who concurred in the decision having asked for rehearing, and a majority of the circuit judges of the circuit in regular active service not having voted for rehearing by the court in banc, the petition for rehearing is denied.

BY THE COURT,

s/ Weis
Circuit Judge

Dated: February 1, 1988

APPENDIX B — ORDER OF THE UNITED STATES COURT OF APPEALS GRANTING MOTION FOR ENLARGEMENT OF TIME

IN THE UNITED STATES COURT OF APPEALS
FOR THE THIRD CIRCUIT

No. 87-5123

TRI-BIO LABORATORIES, INC.,

Appellant,

vs.

UNITED STATES OF AMERICA, and FOOD AND DRUG ADMINISTRATION,

Appellee.

MOTION FOR ENLARGEMENT OF TIME TO FILE PETITION FOR REHEARING

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Appendix B

January 12, 1988

ORDER
Motion GRANTED.

For the Court
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Clerk

APPENDIX C — OPINION OF THE UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT

UNITED STATES COURT OF APPEALS
FOR THE THIRD CIRCUIT

No. 87-5123

TRI-BIO LABORATORIES, INC.,

Appellant,

v.

UNITED STATES OF AMERICA and FOOD AND DRUG ADMINISTRATION,

Appellees.

APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF PENNSYLVANIA

(D.C. Civil No. 86-0083)

Submitted Pursuant To Third Circuit Rule 12(6)
August 19, 1987

Before: GIBBONS, *Chief Judge,*
and WEIS, *Circuit Judge,* and
KELLY,* *District Judge.*

Filed December 29, 1987

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* The Honorable James McGirr Kelly, United States District Judge for the Eastern District of Pennsylvania, sitting by designation.

Appendix C

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Appendix C

OPINION OF THE COURT

WEIS, *Circuit Judge.*

A pharmaceutical manufacturer filed for Food and Drug Administration approval of a generic animal drug, incorporating in its application the research and testing data submitted by another manufacturer that earlier had obtained approval to market the predecessor brand name drug. Because of its policy treating such data as proprietary and confidential, the FDA refused to consider the previously filed material. The district court sustained the agency action and entered summary judgment against the generic manufacturer. We will affirm.

Plaintiff manufactures Gentaject, a veterinary pharmaceutical product recommended for use in one day old chicks to prevent early mortality caused by three species of bacteria.[1] Gentaject, a generic drug,[2] contains the same ingredients as a previously approved product manufactured by the Schering Corporation of Kenilworth, New Jersey and currently marketed under the brand name "Garasol."

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1. The drug is intended to combat Escherichia coli, Salmonella typhimurium, and Pseudomonas aeruginosa in day-old chicks.

2. The term "generic drug" is used throughout this opinion in its broadest possible context: to denote a product not protected by trademark and the non-proprietary name of which is ordinarily descriptive of its chemical composition. *See* Dorland's Illustrated Medical Dictionary 639 (25th ed. 1974). Our definition, therefore, is more expansive than the one set out by the Supreme Court. *Cf.* United States v. Generix Drug Corp., 460 U.S. 453, 454-55 (1983). We adopt our broader definition in light of the plaintiff's assertion that Gentaject is an exact duplicate of Garasol, identical to Garasol in every respect and in all active and inactive ingredients.

Appendix C

Garasol was patented in 1963 and approved for commercial distribution by the FDA in 1978. The patent expired in 1980. A year later, plaintiff sought FDA approval to market its generic copy of Garasol under the brand name Gentaject. As required by statute and FDA regulations, plaintiff filed a new animal drug application (NADA) to demonstrate that its product was safe and effective for its intended use. However, instead of including the extensive test data ordinarily required in new applications, the plaintiffs application merely referred the FDA to Schering's test data in support of the original Garasol application. Because of the plaintiffs failure to submit original safety and effectiveness data, the FDA rejected the application as incomplete.

In October 1982 plaintiff renewed its request for FDA approval, asserting that Gentaject was not a "new drug" requiring the usual panoply of testing. Plaintiff equated its request to a remarketing of a previously FDA-approved drug (Garasol) under a new label (Gentaject). Plaintiff contended that Gentaject, as the bioequivalent[3] of Garasol, in essence already had received FDA approval. But the FDA reaffirmed its denial of the plaintiffs request, citing longstanding agency policy that all new animal drug applications "must stand or fall on the basis of the submitted data."

After some preliminary, inconclusive legal skirmishing, plaintiff agreed to file a citizen's petition[4] with the FDA, requesting

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3. Bioequivalence compares the action of two drugs that, "when administered to the same individual in the same dosage regimen. result in equivalent concentrations of drug in blood and tissue". *Merck Manual* 2241(R. Berkow 14th ed. 1982). *See also* 21 C.F.R. § 320.1(e)(1987).

4. A citizen's petition to the FDA to issue, amend or revoke an (Cont'd)

the agency to declare that Gentaject was not a new animal drug and, thus, did not require a full application. In the petition plaintiff asserted that Gentaject was not a "new drug" within the meaning of the Food, Drug and Cosmetic Act, 21 U.S.C. § 360b(a)(1), because the drug formulation— marketed under the Garasol label — was generally recognized as safe and effective for its intended use by experts qualified to make such judgments.

The Commissioner denied the citizen's petition. The agency concluded that Gentaject was a new animal drug within the meaning of the Act and that it had not become generally recognized as safe and effective.

Plaintiff then brought this action, asking the district court to declare that Gentaject was not a new drug, to direct the FDA to approve its application by incorporating Schering's data, or to reconsider the citizen's petition using the data previously submitted by Schering. Alternatively, plaintiff urged that the FDA approve Gentaject based on agency in-house research — conducted in defense of the litigation — through which it had found Gentaject in fact safe and effective for its intended use. The parties filed cross-motions for summary judgment.

The district court granted the FDA's motion and entered judgment against plaintiff. The court concluded that the FDA properly interpreted its statutory authority in formulating the policy of rejecting applications which depended on data submitted by previous applicants. The court further determined that the

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(Cont'd)
agency regulation or take other administrative action are authorized by 21 C.F.R. § 10.30 (1987). The agency's final resolution of the citizen's petition is, with certain exceptions not relevant here, subject to judicial review.

Appendix C

FDA's rejection of the citizen's petition was not arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law.

On appeal plaintiff argues that the FDA's approach is unreasonable because it compels expensive and indefensible duplicative testing of drugs already approved for commercial marketing. Plaintiff also asserts that the FDA did not adequately analyze all the submitted evidence, a review which plaintiff contends would have revealed that Gentaject was not a "new drug". In the absence of a proper factual hearing by the agency, plaintiff maintains that the district court should have examined the issue de novo.

The FDA responds that plaintiff failed to present the requisite safety and effectiveness data for its product and that, without such evidence, the Food, Drug and Cosmetic Act mandates rejection of the plaintiff's application.

I.

The federal government began premarketing regulation of pharmaceuticals with the Food, Drug, and Cosmetic Act of 1938, Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301-92). After passage of the 1938 Act, FDA approval was necessary before marketing any drug not generally recognized as safe by the scientific community. The Act assumes that a new drug is adulterated and thus unsafe for public distribution until it has been approved. See 21 U.S.C. § § 355(a), 360b(a)(1).

By 1962, however, the FDA had begun approving generic

copies of established "pioneer" drugs[5] without the usual full-scale application ordinarily required for premarketing approval. As to these generics, the FDA concluded that, because the pioneers were generally recognized as safe and were used "to a material extent or for a material time," the regular new drug application was unnecessary. *See* Flannery & Hutt, *Balancing Competition and Patent Protection in the Drug Industry,* 40 Food Drug Cosm. L.J. 269, 272 (1985).

In 1962 Congress amended the Act to require that a new drug applicant establish to the FDA's satisfaction not only the product's safety, but also its effectiveness for the intended use. Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (1962). The retroactive amendments necessitated FDA-retesting of all drugs approved before 1962 for compliance with the new effectiveness standard. To carry out this enormous mandate, the FDA adopted abbreviated procedures. The active ingredients of 4,000 pioneer drug formulations were analyzed. The drugs that survived this scrutiny no longer were considered to be "new drugs" and, thus, were relieved of the arduous, formal reapplication process.

The FDA also decided that a generic drug applicant need not duplicate a pre-1962 pioneer drug's testing; instead, the copycat manufacturer could submit an abbreviated new drug application (ANDA). This abbreviated application need recount only

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5. Pioneer drugs are original drugs which have been approved after compliance with the FDA's rigorous testing requirements. Generic drugs, also known as "copycat" or "me-too" drugs, are copies of the pioneer drugs and can be marketed at reduced prices because their manufacturers have not incurred the developmental and testing costs of the pioneers. *See* United States v. Generix Drug Corp., 460 U.S. 453, 455 n.1 (1983).

bioequivalence and bioavailability,[6] demonstrating that the generic was identical to the pioneer drug.

The FDA's policy differed, however, with respect to generics using formulations of pioneer products approved after 1962. The agency adopted the policy of treating as confidential and proprietary the safety and effectiveness data prepared and submitted by these pioneer drug manufacturers. In the FDA's view, use of this post-1962 research by the agency to review generic drug applications would constitute expropriation.

The FDA's restrictive policy on abbreviated applications thus required generic manufacturers to duplicate many of the pioneers' original testing procedures. The additional expense inherent in this policy necessarily increased the price to consumers of generic drugs. Nevertheless, the FDA feared that appropriation by "me-too" drug manufacturers of data gathered by the pioneer applicants at considerable expense would discourage the development of new products and new uses for existing ones.

Pharmaceuticals for humans and animals were regulated under the same statute until 1968 when Congress recodified the animal drug provisions. Animal Drug Amendments of 1968, Pub. L. No. 90-399, 82 Stat. 343 (1968). After this separation, the FDA continued to impose the same restrictions on abbreviated applications for new animal drugs as it had followed for human drugs.

In 1984, Congress adopted the Drug Price Competition and

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6. Bioavailability is the rate at which and the extent to which the drug enters the general circulation. *See Merck Manual, supra* at 2241; 21 C.F.R. § 320.1(a) (1987).

Appendix C

Patent Term Restoration Act, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified at 21 U.S.C. § 355). This statute attempts to balance the interests of the generic drug manufacturers, who sought to avoid unnecessary testing, against the research investments of the pioneer manufacturers, at the same time mindful of the public need for safe commercial drugs. The 1984 Amendments, which applied only to humam drugs, reflect a statutory compromise of the competing concerns.

The 1984 Act provides an abbreviated application procedure for generic human drugs demonstrating bioequivalency with pioneer drugs approved either before or after 1962. In return, the Act grants pioneer drug manufacturers a statutorily defined period of market exclusivity during which no abbreviated application can be approved. See 21 U.S.C. § 355(j)(4)(D)(i)-(v). This market exclusivity lengthens the pioneer's marketing monopoly beyond the expiration of the drug's patent. In addition, the Act also extends the term of the patent by a period equal to the distribution time lost during the FDA's premarketing testing and approval process. *See* 35 U.S.C. § 156.

As noted earlier, the 1984 Amendments applied only to human pharmaceuticals. The FDA's no-abbreviated application policy remained in effect for animal drugs. Congress was aware of the 1984 Act's limited scope, and bills to similarly revise the animal drugs statute were introduced in both the Senate and House. See S. 2407, 99th Cong., 2d Sess. (1986); H.R. 5069, 99th Cong., 2d Sess. (1986). Congress adjourned before it could act on the legislation, and the animal drug bills were reintroduced in the 100th Congress. H.R. 3120, 100th Cong., 1st Sess. (1987). In the absence of congressional accommodation of these conflicting interests of the generic and pioneer animal drug manufacturers, the FDA's policy continues to protect the pioneers investment

at substantial cost to generic manufacturers.

With this general background in mind, we turn to the merits of the plaintiff's appeal. First, plaintiff challenges the FDA's no-abbreviated application policy contained in 21 C.F.R. § 514.1(a) as an invalid agency interpretation of the congressional mandate. Second, plaintiff asserts that the FDA erred in declaring Gentaject a "new drug" requiring the full panoply of premarket testing.

II.

The plaintiff's objection to the application process rests on the premise that, because the results of the required re-testing are know in advance, the current policy serves no valid scientific purpose. Plaintiff asserts that the FDA practice contravenes congressional intent and lacks a reasonble basis in law.

The principal rationale the agency offers in defense of its policy is that pioneer manufacturers possess a property interest in the test data they present to support their new drug applications. The FDA posits that this proprietary interest may not be appropriated by the government without just compensation. Because the statute indicates no evidence of congressional intent contemplating payment for that interest, no realistic alternative to the policy is evident.

In a statutory arrangement similar to the one considered here, the Federal Environmental Pesticide Control Act, 7 U.S.C. §§ 136-37, requires submission of test data before approval for commercial marketing of a pesticide. In *Chevron Chemical Co. v. Costle*, 641 F.2d 104 (3d Cir.), *cert. denied*, 452 U.S. 961 (1981), the applicant's property interest in the filed research material was at issue. We concluded there that the pioneer manufacturer had

no proprietary right in the requested information because, during the pertinent period, federal law did not create in the submitter a legitimate expectation that the agency would not use the data. The manufacturer was unable to cite persuasive authority that state law on trade secrets would restrict the agency's right to review the pioneer's research data in processing later applications of generic producers.

The Supreme Court was confronted with an aspect of this problem not addressed in *Costle*. In *Ruckelshaus v. Monsanto Co.*, 467 U.S. 986 (1984), a pesticide manufacturer sued to challenge amendments to the federal pesticide law which permitted the agency to consider portions of the pioneer's marketing application when evaluating later submissions by other applicants. The pioneer asserted that the challenged provisions constituted a Fifth Amendment taking, entitling the manufacturer to just compensation.

At the outset, the Supreme Court found that the submitted data constituted a property interest under state law. *See id.* at 1001-04 (citing Restatement (First) of Torts § 757 comment b (1939)). Next, to determine whether the agency's internal reference to one manufacturer's research material for review of another's amounts to a Fifth Amendment taking, the Court considered whether first the manufacturer had a basis for a "reasonable investment-backed expectation" of non-use by the agency. *Id.* at 1005-06. On this point the Court concluded that, in the absence of any "provision of law" proscribing internal agency use, the pioneer could not have had a reasonable expectation that the agency would not consult the submitted data to evaluate applications filed by other manufacturers. *Id.* at 1008. Thus, for data filed in the period during which no federal law protected the material from internal agency use, the Court ruled that such

use would not constitute a "taking" under the Fifth Amendment.

A different result emerged, however, for the time between 1972 and 1978, during which Congress had provided protection against internal agency reference. The Court determined that, for data submitted during this period, Congress had expressly guaranteed pioneers "an extensive measure of confidentiality and exclusive use." *Id.* at 1011. This guarantee, the Court concluded, "formed the basis of a reasonable investment-backed expectation," and agency use for evaluating other applications constituted a taking exposing the government to Tucker Act liability for damages. *Id.*

The *Monsanto* holding is relevant to whether Schering had a protectible property interest here. We anticipated the *Monsanto* variation in *Costle*, commenting that the pioneer manufacturer had "shown us no federal statute preventing internal agency use of the contents of files compiled in the performance of the agency's statutory functions." *Costle*, 641 F.2d at 115. A footnote contrasted this statement to a regulation of the FDA, 21 C.F.R. § 314.1(b) (1980), which prohibited use of agency files to register new human drug compounds without the original registrant's permission. *Id.* at 115 n.26. The cited regulation parallels one adopted in 1971 for use in the animal drug application context. *See* 21 C.F.R.§ 514.1(a) (1987).

The regulation, which memorialized the FDA policy, included the following provision: "Any reference to information furnished by a person other than the applicant may not be considered unless its use is authorized in a written statement signed by the person who submitted it." 21 C.F.R. § 514.1(a) (1987) (originally codified at 21 C.F.R. § 135.4a(a), redesignated to 21 C.F.R. § 514.1(a) by 40 Fed. Reg. 13802, 13825 (1975)). Although in *Monsanto*

the governmental guarantee against internal agency use was grounded on the statute, we are convinced that this agency regulation provided pioneer animal drug manufacturers with an equally reasonable investment-backed expectation that the FDA would refrain from nonconsensual use of research material.

We assume at this point that this regulation was within the FDA's legitimate rulemaking authority, although that factor is not determinative here. As the Supreme Court noted, "the relevant consideration for our purposes is the nature of the expectations of the submitter at the time the data were submitted." *Monsanto*, 467 U.S. at 1013 n. 17. At the time Schering sent its data to the FDA, the regulation had been in effect for some years and had received a consistent intepretation by the FDA, thus entitling Schering to rely on it. Accordingly, the FDA's regulation — as published and implemented — had created for Schering a properly interest in its data. Use of that material in processing the plaintiff's Gentaject application, therefore, would constitute a Fifth Amendment taking, requiring payment of compensation by the government.

Whatever the merits of the argument that before 1971 the FDA had interpreted the Act unreasonably, clearly the agency routinely followed its regulation before 1978, when it approved Garasol. By that time, an investment-backed expectation, perhaps questionable before the 1971 promulgation of the regulation, had ripened into a concrete properly right. Once that interest sprouted, *Monsanto* required the FDA to read the Food, Drug, and Cosmetic Act to support its policy interpretation.[7]

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7. Because the Trade Secrets Act, 18 U.S.C. § 1905, prohibits only public *disclosure* of application data. it does not bar internal agency use of submitted

(Cont'd)

We find nothing in the Act evidencing any intent to have the government compensate the pioneer registrant for the use of its data to review a "me-too" application. Such a procedure would amount to a virtual government subsidy of the generic animal drug manufacturers. The statutory language does not envision such an outcome, nor has plaintiff referred us to any legislative history justifying that result.

In sum, in light of the 1971 regulation, the statute does not now permit the FDA's use of the pioneer manufacturer's data in the processing of the generic manufacturer's new drug application.

III.

As a second argument in support of reversal, plaintiff contends that the FDA erred in classifying Gentaject as a new animal drug. Section 360b requires that all new animal drugs be evaluated on the filing of a complete application consisting of "full reports of investigations which have been made to show whether or not such drug is safe and effective for use." 21 U.S.C. § 360b(b). Plaintiff argues that because Gentaject is an exact duplicate of a previously approved drug, Gentaject is not a "new drug" necessitating the same exhaustive testing as its pioneer.

The Act designates all animal drugs "new" unless they have been "generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness

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(Cont'd)
data. Ruckelshaus v. Monsanto, 467 U.S. 986, 1009 (1984); Chevron Chemical Co. v. Costle, 641 F.2d 104, 115 (3d Cir.), *cert. denied*, 452 U.S. 961 (1981). For the same reason, the plaintiff's reliance on 21 U.S.C. § 331(j) and 21 C.F.R. §§ 20.61, 514.11 is unavailing.

of animal drugs, as safe and effective" and have "been used to a material extent or for a material time." 21 U.S.C. § 321(w). In order to be "generally recognized" as safe and effective, an animal drug must have a general reputation in the scientific community for those properties. "[E]ither the unawareness of the drug product by experts generally or a genuine dispute among qualified experts regarding a drug product's safety and effectiveness preclude its qualifying for exclusion as, generally recognized'." *Premo Pharmaceutical Laboratories, Inc. v. United States,* 629 F.2d 795, 803 (2d Cir. 1980).

This exclusion for "generally recognized" drugs is a narrow one. *Id.* at 802. To establish general recognition, the applicant must produce "evidence consisting of adequate and well-controlled investigations, including field investigation, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug . . . 21 U.S.C. § 360b(d)(3). In addition to this clinical experimentation, the investigation should be "backed by substantial support in scientific literature." *Weinberger v. Bentex Pharmaceuticals, Inc.,* 412 U.S. 645, 652 (1973). The ultimate hurdle of general recognition must be overcome by "substantial evidence." *Weinberger v. Hynon, Wescott & Dunning,* 412 U.S. 609, 629 (1973).

The plaintiff's petition in this case depended heavily on Schering's Garasol data, yet it did not refer to any established body of published literature on Garasol. Moreover, the Commissioner found deficiencies in those materials submitted in support of Garasol's general recognition status. Although these shortcomings played a part in the FDA's denial, it is clear that once the agency properly determined that Schering's proprietary data could not be expropriated to support the plaintiffs petition, the foundation for the citizen's petition collapsed.

Appendix C

After a careful and searching review of the findings of the FDA in rejecting the plaintiffs petition, the district court refused to overturn the denial of the citizen's petition.

We are mindful that in evaluating scientific evidence in the drug field, the FDA possesses an expertise entitled to respectful consideration by this court. *Bentex,* 412 U.S. at 653-54. After a review of the record and the arguments supporting reversal, we are not persuaded to differ with the FDA's decision that the plaintiffs petition did not present adequate scientific evidence to sustain a finding of general recognition.

IV.

Finally, plaintiff points out that the FDA, following its own independent testing performed in connection with the litigation in the district court, has agreed that Gentaject is, in fact, safe and effective for its intended use. This concession, however, does not alter our conclusion.

By its terms, the Act provides no exclusion for new drugs the FDA independently has determined to be actually safe and effective. The only statutory exception available to plaintiff relates to drugs that the scientific community generally accepts as safe and effective. This omission might reflect Congress' desire to avoid burdening the FDA with extraordinary drug testing responsibilities, or simply Congress' preference for conclusions reached by the independent scientific community. Whatever the reason, the statute does not permit approval on the basis of FDA test results.[8]

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8. Approval by the FDA does not transform a new drug into one that is "generally recognized." To be exempt under the general recognition exclusion,

(Cont'd)

Moreover, even if this court could permit plaintiff to rely on the FDA's testing, the petition was nonetheless properly denied. The agency's research was performed after litigation had begun. As a consequence, the drug application, at the time of filing, still lacked the essential prerequisites for approval.

Practical necessity also counsels rejection of the plaintiff's reliance on the agency's data. To hold otherwise would impose on the FDA a new and onerous responsibility. Such a ruling would enable a generic drug manufacturer to circumvent the clear requirements of section 360b by filing an incomplete application which cites the pioneer's data and afterward initiating litigation after FDA denial. The applicant would simply wait for the FDA to conclude its pre-litigation testing, and then point out to the court any favorable, government-financed results. The prohibitive costs of this scenario, both budgetary and in terms of agency personnel, mandate that this option be promptly rejected.

As the Court observed in *Board of Governors of the Fed. Reserve Sys. v. Dimension Financial Corp.*, 474 U.S. 361, 374 n.7 (1986), "[t]he process of effectuating congressional intent at times may yield anomalies," and "the explicit language of a statute" in application may produce "a curious result." Nevertheless, "[n]oting that nothing prohibited Congress from passing unwise legislation, we upheld the enforcement of the statute as Congress had written it." The same reasoning applies here.

(Cont'd)
the drug must have been used "to a material extent or for a material time." 21 U.S.C. § 321(w)(2). The Food, Drug, and Cosmetic Act "is designed so that drugs on the market . . . will have mustered the requisite scientifically reliable evidence of effectiveness long before they are in a position to drop out of active regulation by ceasing to be a 'new drug'." Weinberger v. Hyson, Westcott & Dunning, Inc., 412 U.S. 609, 631 (1973).

Although the result may appear "curious," it is nonetheless compelled.

V.

Although we will affirm the district court and thus will not set aside the FDA's action, we acknowledge the attractiveness of plaintiffs position. Undeniably, the FDA's administration of the Act imposes duplicative expense on generic animal drug manufacturers. We may not, however, overlook the fact that the "me-too" manufacturer seeks to enjoy, without remunerating the pioneer manufacturer, the benefit of the pioneer's substantial investment in research and testing. The consumer may suffer somewhat higher generic drug prices, but, in the long run, will avoid the risk of being denied the pioneer's scientific advances deferred by the prospect of generic manufacturers taking advantage of the developer's labor. Balancing these various factors is a task uniquely suited for legislative resolution, and it appears that the legislation pending in Congress will take up this task.

This case illustrates the classic allocation of power between the legislative and judicial bodies. "[I]n our constitutional system the commitment to the separation of powers is too fundamental for us to pre-empt congressional action by judicially decreeing what accords with 'common sense and the public weal.' Our Constitution vests such responsibilities in the political branches." *Tennessee Valley Auth. v. Hill,* 437 U.S. 153, 195 (1978).

Because the district court properly carried out its function of applying existing law, we will affirm its order.

Appendix C

A True Copy:

Teste:

Clerk of the United States Court of Appeals for the Third Circuit

APPENDIX D — JUDGMENT OF THE UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT

UNITED STATES COURT OF APPEALS
FOR THE THIRD CIRCUIT

No. 87-5123

Tri-Bio Laboratories, Inc.,

Appellant

vs.

UNITED STATES OF AMERICA and FOOD AND DRUG ADMINISTRATION

ON APPEAL FROM THE UNITED STATES DISTRICT COURT FOR THE MIDDLE DISTRICT OF PENNSYLVANIA

Present: Gibbons, *Chief Judge,* and Weiss, *Circuit Judge,* and Kelly, *District Judge**

JUDGMENT

This cause came on to be heard on the record from the United States District Court for the Middle District of Pennsylvania and was submitted pursuant to Third Circuit Rule 12(6) August 19, 1987.

On consideration whereof, it is now here ordered and

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* The Honorable James McGirr Kelly, United States District Judge for the Eastern District of Pennsylvania, sitting by designation.

Appendix D

adjudged by this Court that the judgment of the said District Court entered January 27, 1987, be, and the same is hereby affirmed. Costs taxed against the appellant.

Dated: December 29, 1987

ATTEST

s/ Sally Mrvos
Clerk

Certified as a true copy and issued in lieu
of a formal mandate on February 9, 1988

Test: M. Elizabeth Ferguson
Chief Deputy Clerk, United States Court
of Appeals for the Third Circuit

APPENDIX E — JUDGMENT ORDER OF THE UNITED STATES DISTRICT COURT FOR THE MIDDLE DISTRICT OF PENNSYLVANIA

UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF PENNSYLVANIA

Civil No. 86-0083

Complaint Filed 1/21/86

(Judge Muir)

TRI-BIO LABORATORIES, INC.,

Plaintiff

vs.

UNITED STATES OF AMERICA, et al.,

Defendants

ORDER
January 27, 1987

THE BACKGROUND OF THIS ORDER IS AS FOLLOWS:

Currently pending before us is a report and recommendation of United States Magistrate Raymond J. Durkin filed December 23, 1986 to which on January 12, 1987, Tri-Bio Laboratories, Inc. (hereinafter Tri-Bio) filed objections. When objections are filed to the report of a Magistrate, we must make a *de novo* determination of those portions of the report or specific proposed findings or recommendations to which objections are made. 28

U.S.C. §636(b)(1); Local Rule 904.2. Our review of the Magistrate's report is under the clearly erroneous or contrary to law standard. United States vs. Raddatz, 447 U.S. 667 (1980). After reviewing the Magistrate's report, we may accept, reject, or modify it in whole or in part. 28 U.S.C. §636(b)(1); Local Rule 904.2.

The Food and Drug Administration had determined that Gentaject was a "new drug" and the Commissioner of the Food and Drug Administration upon review affirmed the holding that Gentaject was a "new drug". This case was filed on January 21, 1986 by Tri-Bio seeking a declaration that their drug Gentaject was not a "new drug" within the meaning of 21 U.S.C. §321. If Gentaject is a "new drug" the full panoply of tests and documents required by the Food and Drug Administration comes into effect. After the commencement of suit Tri-Bio filed a motion to amend the complaint and a motion for partial summary judgment. The United States filed its own motion for summary judgment. These motions were referred to Magistrate Durkin. Magistrate Durkin reviewed the record, the material presented to the Food and Drug Administration, the briefs filed regarding the motions before him and held a hearing on the motions. After reviewing all of the material and holding the hearing, the Magistrate recommends that Tri-Bio's amendment of the complaint be permitted and that its motion for partial summary judgment be denied. The Magistrate further recommends that the United States' motion for summary judgment be granted. Tri-Bio contends that the Magistrate erroneously concluded that there is a reasonable basis in the law for the Food and Drug Administration's requirement that new animal drug applicants submit data regarding their "new drug" to the Food and Drug Administration even though the Administration allegedly has similar data available to it from other sources. Tri-Bio also argues

that the Magistrate erred when he concluded that the United States is entitled to summary judgment because *de novo* review of the issues presented to the Food and Drug Administration is not permitted under the facts of this case.

Tri-Bio's objections are technical in nature and obfuscate the essential issue in this case. Tri-Bio has attempted to take a shortcut in its introduction of the drug Gentaject which it avers is exactly the same as a drug manufactured by Schering Corporation known as Garasol which has been approved by the Food and Drug Administration. Because Gentaject is "identical in all respects" to Garasol Tri-Bio insists that it does not have to abide by the full panoplay of Food and Drug Administration rules before it introduces Gentaject to the market. Although we understand Tri-Bio's desire to avoid the lengthy process set up by the Food and Drug Administration for the approval of "new drugs" our task is solely to review the Magistrate's report for error and to see if he applied the correct standard to his review of the Food and Drug Administration's determination. Magistrate Durkin has taken the complex arguments presented by Tri-Bio and the United States and analyzed them thoroughly in his 33-page report to this Court. With that report we find no error. We agree fully with the Magistrate when he states that we are not to substitute our judgment for the judgment of the Food and Drug Administration when reviewing that Administration's decisions. We are merely to look for arbitrary and capricious actions on behalf of the Food and Drug Administration. Unless the Food and Drug Administration's decision was totally unwarranted by the facts it should stand. Citizens to Preserve Overton Park vs. Volpe, 401 U.S. 402 (1971); 5 U.S.C. §706(2)(f). There is no evidence of the Food and Drug Administration acting in an arbitrary and capricious manner and its decision is not unwarranted by the facts. Having found no error with the report of the

Appendix E

Magistrate we shall adopt it as our own and issue the following order.

NOW, THEREFORE, IT IS ORDERED THAT:

1. Tri-Bio Laboratories, Inc.'s motion to amend the complaint is granted.

2. Tri-Bio Laboratories, Inc.'s motion for partial summary judgment is denied.

3. The United States' motion for summary judgment is granted.

4. The Clerk of the Court shall close the file in this case.

5. The Clerk of the Court shall send a copy of this order to United States Magistrate Raymond J. Durkin.

s/ Muir
MUIR, U.S. District Judge

MM:bd

APPENDIX F — REPORT OF MAGISTRATE

IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF PENNSYLVANIA

CIVIL ACTION NO. 86-0083

TRI-BIO LABORATORIES, INC.,

Plaintiff

v.

UNITED STATES OF AMERICA, ET AL.,

Defendants

REPORT OF MAGISTRATE

Before the court are defendants' motion to dismiss or, in the alternative, for summary judgment (Doc. No. 6), and plaintiff's cross motion for partial summary judgment (Doc. No. 24), as well as a motion by plaintiff to amend the request for relief in the complaint. (Doc. No. 19).

Plaintiff, Tri-Bio Laboratories, Inc. (hereinafter Tri-Bio or plaintiff), is a corporation which makes and sells veterinary products. The defendants are the United States of America and its agency, the Food and Drug Administration (hereinafter collectively FDA or defendants), the component agency of the Department of Health and Human Services responsible for regulating the manufacture and distribution of human and animal drugs. In this action, plaintiff seeks judicial review of the FDA's determination, made in response to plaintiff's citizen's petition filed under 21 CFR § 10.30, that plaintiff cannot avail itself, of

an abbreviated procedure for marketing approval of Gentaject, a drug for use in the treatment of one-day old chicks to prevent early mortality caused by certain bacteria, assuming Gentaject is a "new animal drug," or in the alternative, the FDA's determination that Gentaject is a new animal drug.

The defendants' motion to dismiss or for summary judgment was filed on April 3, 1986, together with defendants' statement of material facts and a supporting memorandum to which were attached three appendices. (Doc. Nos. 6-8). On May 6, 1986, plaintiff filed an opposing memorandum, affidavits and other documents, an affidavit of one Shotwell, and a response to defendants' statement of material facts. (Doc. Nos. 12-15). On June 2, 1986, plaintiff filed a reply brief. (Doc. No. 17). By order dated June 17, 1986, the court referred the above motion to the magistrate for report and recommendation.

On June 30, 1986, plaintiff filed a motion to amend request for relief (Doc. No. 19), and on July 9, 1986, filed a brief in support thereof. (Doc. No. 20). On July 17, 1986, defendants filed a brief in opposition. (Doc. No. 21). Although plaintiff's motion to amend the request for relief was not formally referred by the court to the magistrate, following a review of this motion, it was not clear to the magistrate whether its disposition could have some effect on the defendants' motion for summary judgment. In addition, the materials in support of and in opposition to the defendants' motion to dismiss or for summary judgment were voluminous and seemed somewhat complex. As a result, the magistrate decided to hear oral argument which was set for August 27, 1986.

At the hearing, plaintiff, among other things, argued that its complaint raised two broad issues, one legal and the other

factual, and that disputes as to the factual issue rendered summary judgment inappropriate on that issue, for the reasons hereinafter discussed. However, plaintiff indicated that it intended to file a cross motion for summary judgment on what it deemed to be the legal issue in this case. Thus, on August 29, 1986, plaintiff filed a motion for partial summary judgment, a statement of material facts, and a brief which essentially incorporated its arguments on pages 1 through 46 of its brief in opposition to defendants' motion. (Doc. Nos. 24-26). By order dated September 3, 1986, the court referred plaintiff's motion for partial summary judgment to the magistrate. On September 11, 1986, defendants filed their own statement of material facts in response to plaintiff's statement of material facts and a memorandum in opposition to plaintiff's motion for partial summary judgment. (Doc. Nos. 29-30). The latter memorandum contained some additional argument and detail with the result that on September 25, 1986, plaintiff filed a reply brief. (Doc. No. 32).

Subsequently, on October 7, 1986, the defendants filed a motion for protective order against attempted discovery by plaintiff (Doc. No. 34), and on October 27, 1986, the plaintiff filed a motion to extend the period of discovery. (Doc. No. 37). The court denied the former motion on October 10, 1986, and denied the latter motion by order dated November 24, 1986. (Doc. Nos. 36 and 42).

Turning first to plaintiff's motion to amend its request for relief, plaintiff would like to add a request that the court direct the defendant FDA to accept and approve a new animal drug application (NADA) for Gentaject, an animal drug which the FDA has determined to be safe and effective for its intended use. Since a party may amend his pleading once as a matter of course at any time before a rssponsive pleading is served, Rule 15(a), Fed.

R. Civ. P., and since at the time plaintiff filed this motion to amend the defendants had not filed a responsive pleading but rather had filed a motion to dismiss or, in the alternative, for summary judgment, which does not qualify as a responsive pleading, 2A Moore, Federal Practice, ¶ 7.05, the plaintiff could simply have amended the pleading without seeking court approval. Defendants recognize this but argued, among other things, that since court approval was in fact sought, they then had a right to resist that motion, even though the plaintiff need not have proceeded by way of motion. At oral argument, however, it was indicated that the allowance of this motion would not significantly change or alter the defendants' arguments with respect to their motion for summary judgment, and the defendants did not forcefully argue against its allowance. Under these circumstances, the request for relief in the complaint should be deemed amended in the manner set forth by plaintiff.

Turning now to the defendants' motion to dismiss or for summary judgment and the plaintiff's motion for partial summary judgment, both sides indicate that an understanding of the statutory and regulatory framework, as well as the background of this case, is necessary for an understanding of the arguments in support of their motions.

Statutory and Regulatory Framework

As set forth in the defendants' brief (Doc. No. 8), until 1938 federal law did not provide for any kind of pre-market approval of drugs sold in interstate commerce. The Federal Food and Drug Act of 1906 prohibited the interstate distribution of adulterated and misbranded drugs, narrowly defined, but the law lacked any provision to enjoin the distribution of such products. If the Government believed a drug product was unsafe, its only recourse

was to initiate an after-the-fact enforcement proceeding in court to prosecute the distributor or remove the product from the market.

In 1938, Congress enacted the Federal Food, Drug, and Cosmetic Act, 52 Stat. 1040. The most significant feature of the 1938 Act was the establishment of a system for the *pre-market* clearance of drug products. Under the 1938 Act, no "new drug" could lawfully be introduced into interstate commerce unless and until a new drug application (NDA) for that product had been filed with the FDA and became effective. The 1938 Act defined a "new drug" as any product which was (a) not grandfathered (that is, products that were subject to the Federal Food and Drug Act of 1906, and whose labeling remained unchanged, were exempted from the "new drug" provision of the 1938 Act), (b) not "generally recognized" by qualified experts as *safe* for its intended use, or (c) not used to a material extent or for a material time following attainment of general recognition achieved solely as a result of investigation to determine the product's safety.

The 1938 Act did not distinguish between "new animal drugs" and "new drugs." Both types were covered under the provisions of the Act. To obtain approval under the 1938 Act, the manufacturer had to show that its product was in fact *safe* for its intended uses. To enable the FDA to evaluate a product's safety, manufacturers were required to submit specific types of information in their NDA's which included (1) full reports of investigations which have been made to show whether or not such drug is safe for use, and (2) a full description of the methods used in and the facilities and controls used for the manufacturing, processing, and packing of such drug. The 1938 Act contained no provision which permitted one manufacturer to cross reference the data submitted in a competitor's NDA.

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The statute directed the FDA to issue an order refusing to permit the NDA to become effective if, among other things, "(1) the investigation's reports of which are required to be submitted . . . pursuant to subsection (b) of this section do not include adequate tests by all methods reasonably applicable to show whether or not such drug is *safe* . . .; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; . . ."

In 1962, the drug laws were again amended, with a view toward strengthening the laws designed to keep unfit drugs off the market in the first instance and speed their removal should they reach the market. Under the 1962 amendments, manufacturers were now required to show that a "new drug" product was *effective* as well as *safe* for its intended uses. Second, the amendments changed the procedure for obtaining pre-market approval. Under the 1938 Act, NDA's were deemed effective in 60 days unless ths FDA acted affirmatively to reject the application. Under the new amendments, an NDA could no longer automatically become effective; affirmative approval was required. FDA's review time was extended from 60 to 180 days. Under the new legislation, manufacturers seeking NDA approval were required to submit "substantial evidence" of the product's safety and effectiveness. The statute defined "substantial evidence" as "evidence consisting of adequate and well controlled investigation . . . on the basis of which it could fairly and reasonably be concluded . . . that the drug will have the effect it purports . . . to have. . . ." 21 U.S.C. § 355(d). The 1962 amendments also imposed additional obligations on companies which held approved NDA's. Manufacturers were now required to keep records and submit to FDA reports of "clinical experience" that resulted from use of their products following approval.

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The FDA's authority to withdraw approval of NDA's was expanded. The FDA could withdraw approval if, among other things, (1) new information including the "clinical experience" showed that the product was not safe or effective for its intended use or (2) new information showed that the "methods . . . facilities, and controls used for, the manufacture . . . of [the] drug, are inadequate to assure and preserve its identity, strength, quality, and purity. . . ."

The 1962 amendments required FDA to evaluate for effectiveness all drug products, not grandfathered, which had been placed in the market since 1938. Thsse products included not only the approximately 4,000 products that had been specifically approved by FDA, but also those products which had either been distributed illegally by a manufacturer or marketed on the basis of pre-1962 informal FDA advisory opinions that the product was not a new drug. The Government states that because of the enormous administrative burdens created by this mandate, the FDA enlisted the services of the National Academy of Sciences - National Research Council (NAS-NRC) to aid the agency in its review. The FDA requested NDA holders and other interested persons to submit, among other things, a list of literature references that were most pertinent to an evaluation of the effectiveness claims made for their products and related unpublished data. These materials in turn were provided to the NAS-NRC which made recommendations to the FDA regarding the effectiveness of therapeutic classes of products. As FDA reviewed the NAS-NRC recommendations, it published drug efficacy study implementation (DESI) notices in the Federal Register which stated whether classes of products were effective for specific labeled indications.

In 1970, FDA formally adopted an abbreviated new drug application (ANDA) procedure for *human* drug products approved

prior to October 10, 1962, which had been found effective in the DESI review. Under this procedure, manufacturers who did not already hold approved NDA's for DESI-reviewed products were required to file ANDA's to continue marketing their products. Because these drugs as generic entities were regarded as safe and effective, full reports of safety and effectiveness investigations could be omitted from ANDA's. However, manufacturers who filed ANDA's were still required to submit other information including a full statement of ingredients and complete descriptions of manufacturing controls. See 21 CFR § 314.55(a) and (e)(1).

The FDA does not have a *particular regulation* which permits ANDA's to be filed for pre-1962 animal drugs, although ANDA's are permitted to be filed for such products following the procedure established for human drugs.

In the meantime, in 1968, Congress again amended the FDC Act to consolidate into one place in the law all of the principal provisions which relate to pre-marketing clearance of new drugs for administration to *animals*. To effectuate this goal, "new animal drugs" were exempted from one section and separately defined in virtually identical terms in 21 U.S.C. § 321(w). At the same time, a new section was added to describe the requirements for obtaining approval of a new animal drug application. 21 U.S.C.A. § 360. For pioneer drugs, these requirements are identical with requirements relating to NDA's for human drugs. Compare 21 U.S.C. § 355(b)-(d) with § 360b(b)-(d). Finally, new animal drugs were exempted from the FDC Act's food additive provision, see 21 U.S.C. § 321(s)(5), and the requirements necessary to obtain and maintain approval for animal drugs used in human food were transferred to 21 U.S.C. § 360b. *See* 21 U.S.C. § 360b(5), (7) and (8), (d)(F) and (H).

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In September 1984, the drug provisions of the FDC Act were again amended by the Drug Price Competition and Patent Term Restoration Act of 1984. The Government states that this represented a compromise by which Congress sought to balance the consumer's need for lower priced drug products with the manufacturer's need to receive a sufficient return on its investment to develop new products and improve existing products. Under the new law, manufacturers of generic copies of approved pioneer human drug products may file abbreviated NDA's, that is, ANDA's, which rely on specified items of information contained in the pioneer application. Thus, if the generic product is the same as the pioneer, that is, is bioequivalent and has the same active ingredients, labeling, conditions of use, route of administration, dosage, form, and strength, and does not interfere with a valid packet,it may be approved without submitting full reports of clinical investigations to demonstrate safety and effectiveness. The Government states, however, that those amendments did not alter the manufacturer's existing obligation to include in its ANDA all of the other specified information relating to such things as components, composition, and methods of manufacture. The Government states that in exchange for permitting some generic products for human use to be approved on a showing of bioequivalency with the pioneer product, Congress granted exclusive marketing rights during which ANDA's could not be submitted and in some cases extended the patent life of affected products to partially compensate for marketing time that was lost while the product was undergoing FDA's pre-market review procedure. This Act did not affect *animal* drugs.

Factual Background of this Case

In 1978, FDA approved an NADA for Garasol, an injectible drug product which contains gentamicin sulphate as the sole active

ingredient, and which is recommended for use in one-day old chicks to prevent early mortality caused by three specific organisms. The holder of this NADA is Schering Corporation. Garasol is the only gentamicin sulphate product approved by FDA for use in one-day old chicks. In August 1981, plaintiff submitted an NADA for the marketing of a drug manufactured under the trade name, Gentaject. Plaintiff contends that this is an exact duplicate of Garasol, a drug originally patented by Schering in May 1963 which patent expired in May 1980. Plaintiff states that this is an exact duplicate of Garasol which was approved by the FDA as both safe and effective in *1978*, and the Government admits that Gentaject contains the same active and inactive ingredients, bears the same labeling, and is bioequivalent to Garasol. (Doc. No. 8, p. 17). In its NADA seeking the pre-marketing approval of Gentaject, plaintiff made reference to the FDA's prior determination of the safety and efficacy of Garasol as being supportive of the safety and efficacy of Gentaject. In so doing, plaintiff, in effect, was attempting to use an abbreviated NADA procedure to avoid the necessity of performing duplicate tests to prove safety and effectiveness.

By letter dated January 15, 1982, the FDA indicated that it would not accept the NADA for filing because it was incomplete in that, among other things, it failed to provide *full reports of investigations establishing the safety and efficacy of Gentaject as required by 21 U.S.C.* § 360b(b)(1), in addition to other deficiencies, including the fact that the NADA did not contain complete information relating to the manner in which the product would be manufactured, human safety data, and the like. In a letter dated October 15, 1982, plaintiff again requested the FDA to permit plaintiff to rely on information of the safety and efficacy of Garasol as supporting the safety and efficacy of Gentaject. It was pointed out that plaintiff was in the process of obtaining

a test establishing that Gentaject is the biological equivalent of Garasol and should the FDC require any further reasonable data regarding safety and effectiveness, plaintiff would attempt to comply therewith, *notwithstanding* its position that Gentaject is *not* a new animal drug. It was pointed out, however, that should reasonable protocols be not established within a short period of time, plaintiff intended to market Gentaject without FDA approval.

By letter dated January 5, 1983, the FDA again denied this request, noting that gentamicin sulphate was approved for use in animals after 1962, and that for drugs approved after 1962, the agency's longstanding interpretation of the requirements imposed in the drug amendments of 1962, which in turn were adopted in the animal drug amendment of 1968, is that the new animal drug application for a drug that *was not reviewed by the NAS-NRC and that was marketed only after the 1962 drug amendments* must stand or fall on the basis of the submitted data, and those data must be evaluated under current standards.

In March 1983, the Government filed a seizure action against a quantity of Gentaject stored at a business of plaintiff's distributor located in Arkansas. The complaint alleged that the product was an unapproved "new animal drug." Because neither Tri-Bio nor anyone else filed a claim to the article, default was entered and the goods were condemned and destroyed.

On April 23, 1983, Tri-Bio filed a complaint in this court seeking a declaration that Gentaject was not a "new animal drug," and an injunction prohibiting FDA from taking any further regulatory action against plaintiff for Gentaject based on the "new animal drug" charge. During that litigation, the parties executed a statement of undisputed facts which, among other things,

indicated that Gentaject is identical in all respects to Garasol which was previously approved by the FDA in 1978 as being a safe and effective animal drug when used in accordance with its labeling, and that Gentaject is similarly safe and effective for such use. Notwithstanding these admissions, however, the FDA continued in its assertion that Gentaject could not be marketed.

In July 1984, the parties agreed to voluntarily dismiss their respective cases so that Tri-Bio could file a citizen's petition with the FDA seeking administrative declaration that Gentaject was not a new animal drug. To facilitate the filing of the petition, the FDA agreed not to institute any enforcement action against Tri-Bio, its officers, or Gentaject for a period of 18 months. The citizen's petition was filed with the FDA on September 13, 1984. In the petition, Tri-Bio contended that Gentaject need not be pre-cleared by FDA because Gentaject's approved twin, Garasol, is generally recognized as safe and effective. In support of its petition, Tri-Bio submitted labeling and formulation data for Gentaject; reprints of published reports; summaries, abstracts, and bibliography of other papers bearing upon the safety and effectiveness of gentamicin sulphate, the active ingredient in Garasol and Gentaject; and two affidavits of experts who assert that Garasol was generally recognized as safe and effective for its intended use. The Government states, however, that Tri-Bio did not submit any *published literature* which mentioned Gentaject.

By letter dated September 17, 1935, the FDA denied Tri-Bio's petition. The Commissioner reviewed the materials submitted by plaintiff and concluded that they were not adequate to show that Garasol or Gentaject are generally recognized as safe and effective for their intended uses, and the Commissioner ruled that both products are new animal drugs, and that Gentaject could not be marketed without prior FDA approval of an NADA

containing full safety and effectiveness data.

This lawsuit ensued on January 21, 1986, seeking a declaration that Gentaject is not a "new drug" within the meaning of 21 U.S.C. § 321(w), an order directing the FDA to accept and approve the NADA application for Gentaject which relies, in whole or in part, on the safety and effectiveness data contained in the NADA file by Schering with respect to Garasol, and an order directing the FDA to reconsider the citizen's petition filed by plaintiff based upon full review of all data and information available to it, including data submitted to the FDA by Schering in the NDA files for Garasol.

Discussion

Plaintiff characterizes its complaints as raising two broad issues, one factual and the other legal. It describes the legal issue as whether the FDA has abused its discretion by demanding that Tri-Bio perform unnecessary duplicative tests to prove what it already knows and has admitted, that Gentaject is a safe and effective animal drug when used in accordance with labeling. In effect, plaintiff would like the Act construed in such a way as to permit an abbreviated procedure for approval of new animal drug applications for generic copies of pioneer *animal* drugs even though the pioneer drug was approved after 1962, a procedure subsequently enacted into law in 1984 for new *human* drugs.

Before addressing plaintiff's argument with regard to this legal issue, the statutory requirements will be set forth.

21 U.S.C. § 360b(b)(1) requires a sponsor of an NADA for an animal drug to submit, *inter alia,* to the FDA "full report of investigations which have been made to show whether or not

such drug is safe and effective for use." Under § 360b(d)(1)(A), the Secretary may refuse to approve the application if the investigations, reports of which are required to be submitted to the Secretary pursuant to § 360b(b) do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof. Moreover, proof of a drug's efficacy must be supported by "substantial evidence . . . consisting of adequate and well controlled investigations, including field investigations by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved. . . . 21 U.S.C. § 360b(d)(3). In addition, § 360b(d)(1) provides in pertinent part that the Secretary can *refuse* to approve the application for various other reasons, including:

> "(D) Upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions;
>
> "(E) Evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the condi tions or use prescribed, recommended, or suggested in the proposed labeling thereof;
>
> "(F) Upon the basis of the information submitted to him as part of the application or any

> other information before him with respect to such drug, the tolerance limitation proposed, if any, exceeds that reasonably required to accomplish the physical or other technical effect for which the drug is intended."

Tri-Bio admits that it has not submitted to the FDA the required "full reports of investigations" for Gentaject which have been made to show whether Gentaject was safe and effective for use, but rather, that it has relied upon "the prior determination of safety and efficacy of the composition of Garasol as being supportive of Gentaject's safety and effectiveness." (Doc. No. 15, ¶ 3).

Since both plaintiff and defendants are seeking summary judgment on this legal issue, the discussion will center on plaintiff's arguments and FDA's response. Plaintiff's argument assumes for the purposes of this legal issue that Gentaject is a new animal drug. As hereinafter discussed, on the "factual issue," plaintiff argues in the alternative that it is not a new animal drug.

Plaintiff argues that the above statutory provisions do not require a new animal drug applicant to duplicate clinical studies to establish safety and efficacy, but the FDA's policies, arising from an interpretation of the statute, require just that, in that the FDA will accept the abbreviated NADA procedure for generic copies of pioneer drugs approved prior to October 10, 1962; it will not for drugs approved after 1962 (one of which is Garasol); and even has a third policy for a few post-1952 drugs which have tests published in scientific journals.

More specifically, plaintiff argues that under § 360b(d)(1)(D), (E) and (F), in approving a new animal drug, the FDA shall

consider not only the information submitted as part of the NADA, but "any other information before the FDA." Plaintiff argues that "any other information" encompasses many sources and that FDA may use its own knowledge or its own prior test results.

However, the sections cited do not require the FDA to look at any information it has, but rather, refer to "any other information" before the agency has an appropriate basis for *refusing* to approve the application, and not for approving it. It is not up to the FDA to make a case for the applicant, although it need not ignore any information within its knowledge which may raise questions as to the efficacy of the drug.

Plaintiff argues that the abbreviated approval process (ANDA) makes sense, but argues that the court is confronted with two diametrically opposed statutory interpretations posited by the FDA. Plaintiff argues that with respect to pre-1962 drugs, FDA claims that it has discretion to interpret § 360b a not requiring the duplicate drug applicant to prove safety and effectiveness, and with respect to post-1962 drugs, FDA claims that it has discretion to interpret the statute as requiring the duplicate drug applicant to perform unnecessary duplicative clinical testing to prove safety and effectiveness. Plaintiff argues that the FDA's diametrically opposed interpretations of the Act revolve around the October 10, 1962, demarkation date which has no basis in the Act, which has a unitary approval scheme applicable to all new drugs. Plaintiff argues that the sole basis which the agency has advanced as sanctioned for its distinction for pre- and post-1962 drugs is the DESI review which has nothing to do with any alleged differences between ANDA's for pre-1962 versus post-1962 drugs. Plaintiff argues that DESI was not established for anything relating to ANDA's since ANDA's were not even instituted until 1970, years after the DESI program began.

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It appears, however, that the FDA's interpretation of the Act as regards pre-1962 and post-1962 drugs has a basis in the Act, that this distinction has been at least impliedly acquiesced in by Congress when in 1984 it enacted subsequent legislation to incorporate into law the abbreviated process for pre-1962 or post-1962 new drugs for human use, and is only now addressing that distinction as it relates to new *animal* drugs.

As noted above, prior to 1962 an NDA was approved if the drug was safe. However, the 1962 amendments brought into the picture the question of effectiveness, as well as safety. Thus, the FDA was faced with evaluating all new drug products not grandfathered which had been placed on the market since 1938, which included not only the approximately 4,000 products that had been specifically approved by FDA, but also those which had been manufactured or marketed on the basis of pre-1962 informal FDA advisory opinions that the product was not a new drug.

This presented the FDA with the task of evaluating 16,500 claims made on behalf of 4,000 drugs. *See* Warner Lambert Co. v. Heckler, 3 Cir. 1986, 787 F. 2d 147, 149. To aid in this task of fulfilling the statutory mandate, the FDA retained NAS-NRC, Weinberger v. Hynson, Westcott & Dunning, 1973, 412 U.S. 609, 614, and based on a review of the recommendations, it published the DESI notices. Hence, the DESI was in reaction to a solution of a large problem. However, the Act still required the FDA to determine the safety and effectiveness of post-1962 drugs, and thus, the DESI procedure for post-1962 drugs was not necessary. Thus, it cannot be said that the FDA's actions regarding pre- and post-1962 drugs had no basis in the Act.

In 1970, FDA formally adopted the new ANDA procedure

for *human* drug products approved prior to October 10, 1962, which had been found effective in the DESI review. As defendants argue, Congress apparently recognized and acquiesced in the FDA's determination that abbreviated applications are not acceptable for post-1962 *animal* drugs in that the Drug Price Competition and Patent Term Restoration Act of 1984 amended the Act to provide for abbreviated applications for any generic copy of a previously adopted pre-1962 or post-1962 new drug for *human* use. However, this did not apply to new animal drugs. Although plaintiff argues that this difference could relate "solely to the failure of the generic animal drug industry to effectively overcome the lobbying efforts of the large pioneer animal pharmaceutical manufactuiers," rather than to "any perceived legislative distinction between animal and human drugs this appears to be pure speculation, and nothing is offered to back up such an argument. Moreover, the fact that the FDA continued to interpret the Act properly as it applied to animal drugs is apparent from legislation currently pending in Congress to amend the Act to establish for animal drugs the same abbreviated procedure that was established in 1984 for drugs for human use.

In summary, the FDA's administration of the Act from 1938 to 1962, its reaction to the problems created by the 1962 amendments, its subsequent adoption of the abbreviated ANDA policy for pre-1962 drugs, Congress' apparent acquiescence in the FDA's administration and interpretation of the Act as reflected in the 1984 legislation in which it built in an abbreviated procedure for post-1962 as well as pre-1962 *human* drugs, and the pending legislation to provide for the same procedures for animal drugs as did the 1984 procedures for human drugs, would indicate that FDA has been properly interpreting the Act insofar as not permitting the abbreviated process for post-1962 pioneer drugs for animals.

Thus, on the legal issue, it appears that summary judgment could properly be entered in favor of the defendants. However, the inquiry does not end there because plaintiff, while apparently conceding that Gentaject could be considered a new drug for purposes of its legal argument, contends in the alternative that Gentaject is generally recognized by experts as safe and effective and, therefore, not a "new animal drug" within the meaning of 21 U.S.C. § 321(w). Plaintiff describes this as the "factual issue."

Section 321(w) provides that to escape classification as a new animal drug, Gentaject must both be generally recognized by experts as safe and effective, and have been used to a material extent and for a material time. It has been held that general recognition of a product's safety and effectiveness must be based on a substantial body of reliable, published studies, Weinberger v. Bentex Pharmaceuticals, Inc., 1973, 412 U.S. 645, 652, and that the "generally recognized" exception to the Act's new drug clearance procedure is a "very narrow one." Premo Pharmaceutical Laboratories, Inc., v. United States, 2 Cir. 1980, 692 F. 2d 795, 802.

Plaintiff argues that there are material facts in dispute as to this issue. Before identifying the factual issue, plaintiff's argument becomes somewhat sophisticated. Plaintiff argues that before the court can determine whether any genuine issues of material *fact* exist, the court must necessarily first determine what *legal* issues are in the case so that it can be demonstrated what facts are material to a consideration thereof. Plaintiff argues that the Government frames the issue in this case as an attack on its broad administrative discretion to determine new animal drug status, and argues that there is no genuine issue of material fact because the Commissioner's decision denying Tri-Bio's citizen's petition was not arbitrary and capricious. Plaintiff argues,

however, that the Government's characterization of the appropriate standard of review is mistaken.

In that connection, plaintiff argues that although it is a general rule that an agency action may be set aside if the action was arbitrary or capricious, an abuse of discretion, or otherwise not in accordance with the law, in certain narrowly defined circumstances such as are presented in the instant case, the Administrative Procedures Act requires the reviewing court to engage in a de novo review of the action and set it aside if it is "unwarranted by the facts." 5 U.S.C. § § 706(2)(F), 1976. Plaintiff cites authority for the proposition that de novo review is authorized when agency action is adjudicatory in nature, and the agency's fact finding procedures are inadequate. Plaintiff argues that there can be little question that the Commission, in denying Tri-Bio's citizen's petition, was adjudicatory in nature. Plaintiff argues that additionally, the fact finding procedures used to determine whether Gentaject was or was not a new animal drug were grossly inadequate. Plaintiff notes that in denying its citizen's petition, the FDA never expressly declared Gentaject to be a new animal drug requiring premarketing NADA approval, and made no factual findings which would support such a declaration. Plaintiff argues that the FDA merely reviewed the materials submitted by Tri-Bio and concluded that they were inadequate to show that either Garasol or Gentaject is generally recognized as safe and effective for its intended uses. Tri-Bio also argues that it was never made aware of a perceived need to supplement the petition until after the alleged defects were identified and the ruling was made. In that connection, Tri-Bio argues that a petition may only be supplemented following a ruling only with the approval of the Commissioner; that it was never requested to attend any conferences or meetings in connection with the petition and FDA's ruling; and that in any event, whether a hearing should

be held is merely discretionary. Tri-Bio argues that it was, therefore, unable to offer further evidence, was precluded from cross-examining FDA's experts, and that the agency's fact finding procedures are, therefore, woefully inadequate which would indicate that a *de novo* hearing is required under 5 U.S.C. § 706(2)(F). Tri-Bio argues that there is no administrative record on the issue of the "new drug" status of Gentaject and the sole administrative record which is before the court deals only with the FDA's findings, conclusions, and rationale, why Tri-Bio's citizen's petition failed in the judgment of the FDA to establish the "old drug" status of Gentaject.

However, filed with the court as Apoendix C to defendants' brief in support of their motion for summary judgment is the completed administrative record of the FDA's consideration of Tri-Bio's petition for a determination that Gentaject is not a new animal drug. As defendants argue, FDA's regulations placed Tri-Bio on notice to present the full factual and legal basis in its petition for its claim that Gentaject is not a new animal drug. 21 CFR § 10.30(b)B. 21 CFR § 10.30(i) delineates the contents of the administrative record and 21 CFR § 10.30(j) provides that "the administrative record specified in paragraph (i) of this section is the exclusive record of the Commissioner's decision." The record indicates that the FDA addressed plaintiff's petition in great detail and found certain deficiencies. In its responsive statement of facts, ¶¶ 5(a)-(e), (g), plaintiff has admitted a number of these deficiencies. Before setting forth the deficiencies, the first paragraph of the decision states that Tri-Bio's petition to declare that Gentaject is not a new animal drug is denied.

Although plaintiff argues that it was never made aware of the perceived need to supplement the petition until after the alleged defects were identified and the ruling made, and even then such

supplementation is in the discretion of the Commissioner, the mere fact that discretion is vested in the Commissioner would not make the fact finding process inadequate. Further, the Commissioner may at any time reconsider a matter and the regulation describes what the Commissioner considers in deciding whether to reconsider. 21 CFR § 10.33. These fact finding procedures have been held to be adequate. Upjohn Manufacturing Co. v. Schweiker 6 Cir. 1982, 681 F. 2d 480. It appears, therefore, that the standard of review is whether the FDA's action was arbitrary and capricious.

Plaintiff argues, however, that notwithstanding the standard of review, certain cases have held that it is error for a district court not to entertain declaratory action on a product's new drug status. They argue that the status of a drug as "new" is clearly a factual issue which cannot be resolved by a motion for summary judgment on the basis of the present record. Defendants in their reply brief do not appear to directly address the cases cited by plaintiff. However, the magistrate is not convinced that just because declaratory relief is sought, this would permit the court to hear additional evidence or go beyond the administrative record. One of the cases cited by plaintiff which arose in this Circuit is United States v. Articles of Drug . . . Hormonin, D. N.J. 1980, 498 F. Supp. 424, *aff'd* mem. 3 Cir. 1981, 672 F. 2d 902, 904. Plaintiff argues that the district court held that it could determine "new drug" status despite a contention that the Government had not first produced an administrative record for review which was sufficient to justify its conclusion that the drug product was a new drug. However, that action was filed by the United States for forfeiture on the basis that the drug involved was a new drug which was subject to pre-marketing approval. The manufacturer moved for a preliminary injunction against further seizures of the products and requested a remand to the FDA for development of an administrative record. The district court's decision did not

indicate why the motion for remand was denied. However, the district court did point out that while a district court is empowered to adjudicate the "new drug status" of a given drug product, its inquiry is limited to the question of "general recognition" and is not empowered to evaluate the actual safety and effectiveness of a drug product, a determination which is committed to the FDA. The court also noted that a general dispute concerning the unawareness of the drug product among qualified experts precludes a finding of "general recognition" which must also be based on adequate and well-controlled investigations and publication in scientific literature. Thus, in *United States v. Articles of Drug . . . Hormonin, supra,* no questions had been adjudicated by the FDA on a formal presentation by plaintiff. As hereinafter discussed, in the instant case these decisions have been made by the FDA after plaintiff submitted the questions to the FDA through a citizen's petition filed pursuant to a stipulation which ended the prior litigation between the parties. Under these circumstances, it does not appear that the court should deviate from the general rule that a reviewing court may only determine whether the decision was based on a consideration of the relevant factors and whether there has been a clear error of judgment. Although this inquiry into the facts is to be searching and careful, the ultimate standard of review is a narrow one. The court is not empowered to substitute its judgment for that of the agency. Citizens to Preserve Overton Park, Inc. v. Volpe, 1971, 401 U.S. 402. In order to overturn the FDA's determination as arbitrary or capricious, this court must find that FDA's determination that Gentaject is a new animal drug due to its lack of general recognition as safe and effective constitutes a clear error of judgment. Weinberger v. Bentex Pharmaceuticals, Inc., *supra.* The court's function is to take a second look at the same administrative material, not a redoing. Doe v. Devine, D. D.C. 1982, 545 F. Supp. 576, 584, n. 9, *aff'd.* D.C. Cir. 1983, 703

F. 2d 1319; *See also Upjohn, supra.*

Moreover, the "declaration" that plaintiff seeks would have to be not only on evidence presented to the FDA, but also on new evidence and then only if the court interprets § 321(w) as permitting, contrary to the FDA's interpretation, non-new drug determinations on the basis of a lesser quality and quantity of evidence than required for approval of a product in the first instance. As hereinafter discussed, the magistrate believes that FDA's interpretation of § 321(w) to be correct.

In that connection, plaintiff argues that the FDA's contention that it correctly denied the citizen's petition on the basis of the evidence submitted in support of the petition is inadequate to establish that Gentaject is generally recognized as safe and effective for its intended use, is based on a clearly unreasonable interpretation of the applicable statutory sections. Plaintiff argues that a reviewing court must first determine whether the FDA's construction of the applicable statute is "reasonable" and then whether its application withstands the arbitrary and capricious standard of review of the Administrative Procedures Act. Plaintiff argues that if the agency unreasonably interpreted the applicable statute, its application to the *facts* must necessarily have resulted in arbitrary and capricious findings and conclusions.

Plaintiff argues that the Government contends that there are three criteria which a drug product must meet before it may qualify for the "generally recognized" exemption under § 321(w). First, the safety and effectiveness of the product must be "generally recognized" by qualified experts, that the focus of an inquiry regarding a product's general recognition is not to determine safety and effectiveness at all, but to ascertain the drug's general reputation in the scientific community for such characteristics,

and that whether or not a particular product or its duplicate is actually safe and effective, or has been approved by the FDA, is irrelevant in determining whether the product or its duplicate is generally recognized as safe and effective. Second, the safety and effectiveness of the product must be documented by the same quality and quantity of evidence that is necessary to obtain approval for the product in the first instance under § 360b(d) and § 355(d). In that connection, the statute requires substantial evidence of the product's safety or effectiveness, that is, evidence consisting of adequate and well controlled investigations, including field investigations on the basis of which it could fairly and responsibly be concluded by experts that the drug will have the effect it purports or is represented to have. Third, general recognition must rest on a foundation of "controlled clinical experimentation backed by substantial support and scientific literature," that is, published material.

Plaintiff argues, however, that the FDA's position that whether or not a particular product or its duplicate is actually safe and effective or has been approved by the FDA is irrelevant in determining whether the product or its duplicate is generally recognized as safe and effective, is a misconstruction of the statute based on a narrow reading of Weinberger v. Hynson, Wescott & Dunning, *supra,* and Weinberger v. Bentex Pharmaceuticals, Inc., *supra.* Plaintiff argues that in the former case, the court held, "We cannot construe [§ 321(w)] to deprive FDA of jurisdiction over a drug which, if subject to FDA regulation, could not be marketed because it did not pass the 'substantial evidence test' [in 360b(d) and 355(d)]" and due to the statement in the latter case that " . . . as we indicate in Hynson, supra, at 631, the reach of scientific inquiry under both [§§ 360b(d) and 321(w)] is precisely the same." Plaintiff argues that the FDA thus concluded that the safety and effectiveness of the product must

be documented by the same quantity and quality evidence that is necessary to obtain approval for the product in the first instance. Plaintiff argues, however, that in *Hynson*, the court was concerned with the deregulation of a drug which could not pass the "substantial evidence" test, whereas there is no similar concern in the instant case, in that the FDA admits Gentaject to be safe and effective for the label indications. While recognizing that general recognition must be established through *reputation* in the scientific community, plaintiff argues that actual safety and efficacy of a drug is clearly relevant to such inquiry, and that under the FDA's interpretation, it would be virtually impossible for a drug to transcend new drug status since the FDA would require the expert consensus as to the safety and efficacy of a drug be based solely on the *published literature*. Plaintiff argues that FDA subjected each piece of scientific literature in finding there was no scientific literature supporting the general recognition of Gentaject, and refused to consider the literature submitted with regard to Garasol despite its acknowledgement that they were identical in composition. Plaintiff argues that the FDA also chose to ignore the affidavits of independent experts as to the general recognition of the composition of the products as safe and effective. Plaintiff argues that it admits that the *trade name* Gentaject is not generally recognized by qualified experts as being safe and effective, but that the composition of Gentaject has already been approved by the FDA as safe and effective through its approval of Garasol of which Gentaject is a generic copy. While recognizing that that determination is not dispositive as to the issue of general recognition, plaintiff argues that it provides a foundation on which expert opinion can be based. Plaintiff argues that even assuming that the FDA properly concluded that each submission does not establish the requisite showing of the non-new drug status of Gentaject, the FDA acted arbitrarily and capriciously in giving this evidence no weight whatsoever. Plaintiff

argues that it is important to note that none of the courts examining the issue of general recognition have been confronted with the precise issue raised, since in no prior case has FDA admitted, as it has in the instant case, that Gentaject is identical in composition, bioequivalence and bioavailability to a previously approved drug.

Tri-Bio states, therefore, that in any evidentiary hearing before this court, it intends to produce expert testimony that in addition to being actually safe and effective, the composition of both Garasol and Gentaject is generally recognized as safe and effective by a consensus of experts qualified by scientific training, and that this testimony will be supported by scientific literature regarding the safety and efficacy of gentamicin sulphate generally. Plaintiff states that it will also provide literature supporting the safety and efficacy of Garasol. Plaintiff states that the expert consensus will be based upon their knowledge that the composition of the drug products is actually safe and effective as determined by the FDA and evidenced by the NADA approval of Garasol, and the summary of specific tests establishing safety and efficacy published in the Freedom of Information summaries. In the latter connection, plaintiff states that although the information in the summaries does not in and of themselves establish the general recognition of a drug, it is something upon which trained experts can base their opinions, just as they can base their opinions on the FDA's approval of Garasol and the like.

Finally, plaintiff contends that proof of the general recognition of the safety and effectiveness of the composition of Gentaject will not end the inquiry since to be classified as an old drug, it must further be established that the "drug has been used to a material extent or for a material time" under the conditions prescribed, and that this, too, is a factual issue that cannot be

avoided by a motion for summary judgment on the present record.

Thus, in this third prong of plaintiff's "factual issue" argument, plaintiff would have this court reject the FDA's construction of the law that to escape classification as a new animal drug, plaintiff must show that Gentaject is generally recognized by experts as safe and effective based on the same quality and quantity of evidence that is necessary to obtain approval for the product in the first instance; find that FDA's application of the evidence presented to it by plaintiff to that construction of the law, therefore, to be arbitrary and capricious,; and then, accepting plaintiff's less restrictive interpretation of the requirements of the law, find on a *de novo* basis that Gentaject is not a new drug based upon the evidence submitted to the FDC, evidence, although not submitted, that is known to the FDC, and evidence in the way of expert testimony and documentary evidence not presented to the FDC to support the claim that Gentaject is not a new animal drug.

The magistrate, however, does not believe that the evidentiary standard insisted upon by the FDA is not in keeping with the law. Plaintiff recognizes that in both *Hynson* and *Bentex*, the Supreme Court has held that it could not construe § 321(w) to deprive FDA of jurisdiction over a drug which, if subject to FDA regulations, could not be marketed because it could not pass the substantial evidence test in §§ 360b(d) and 355(d), and that the reach of scientific inquiry under both 360b(d) and 321(w) is precisely the same. Although plaintiff points to certain additional language in *Bentex* to the effect that "it *may* be true . . . that in some cases general recognition that a drug is effective might be made without the kind of scientific support necessary to obtain approval of an NDA," the Supreme Court did not indicate what type of case that may be and it is only plaintiff's argument that

the above statement, not necessary to the disposition of *Bentex*, indicates that this is the type of case. However, in view of the plain language in the Supreme Court decisions, the magistrate cannot say that the FDA is misconstruing the law.

On that basis, therefore, the question of whether Gentaject is a non-"new drug" should be viewed in light of the administrative record developed before the FDA on plaintiff's citizen's petition. *Upjohn, supra.* Although plaintiff states that Gentaject is a generic copy of Garasol, the Act's "new drug" provisions regulate products, not active ingredients, and a product may not avoid the Act's pre-market clearance provisions solely upon the general recognition of its active ingredients. United States v. Generix, 1983, 460 U.S. 453. As noted above, Tri-Bio has admitted the deficiencies pointed to in the FDA's decision, including that it did not submit any published literature at all that mentions Gentaject, that the one study that dealt with Garasol on which plaintiff would like to rely did not show that Garasol was administered at its optimal dosage; that the one study using gentamicin sulphate in accordance with Garasol's labeling had no statistical analysis and did not discuss toxicity of Garasol to humans or the nature of any Garasol metabolites that might remain in edible tissues of animals treated with Garasol; that one study of gentamicin sulphate in the treatment of Salmonella Typhimurium in young chicks used dosages far in excess of those recommended in Garasol's labeling and administered those doses at times different than recommended in Garasol's labeling; that the three abstracts of paper submitted by Tri-Bio provided no information about the design of the studies, controls, if any, the details of the studies, or the number of animals used; that the six papers that reported on uses of gentamicin sulphate different from those recommended in Garasol's labeling or that reported on products other than Garasol containing gentamicin sulphate

did not study Garasol and its specific uses; and that neither of the affidavits submitted by Tri-Bio cited a single study to support the opinion that Garasol is generally recognized as safe and effective. neither affidavit stated whether any study which was alluded to but not cited contained substantial evidence consisting of adequate and well controlled investigations, and neither affidavit expressed the opinion that Gentaject is generally recognized as safe and effective. with respect to the new evidence that plaintiff attempts to bring before this court, that evidence should have been presented to the FDA. It is recognized that if that evidence is submitted to the FDA, under the FDA's construction of the Act, it would undoubtedly be rejected on the basis that it would not be of the same quality and quantity of evidence that is necessary to obtain approval of the product in the first instance. However, if the Act is to be changed to permit a showing of non-"new drug" status through what amounts to another abbreviated procedure, that should be for Congress.

Further, in view of these admissions of the manner in which its petition was lacking, it cannot be said that the FDA's denial of the citizen's petition was "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." As noted above, to make this finding, the court must consider whether the decision was based on a consideration of relevant factors and whether there has been a clear error of judgment. Although this inquiry into the facts is to be searching and careful, the ultimate standard of review is a narrow one, and the court is not empowered to substitute its judgment for that of the agency. *Citizens to Preserve Overton Park v. Volpe;, supra.* In view of plaintiff's admissions with respect to the deficiencies in their submission, it cannot be said that this is arbitrary and capricious action.

Appendix F

On the basis of the foregoing, it is respectfully recommended that:

(1) Plaintiff's amendment of the complaint be permitted;

(2) Plaintiff's motion for partial summary judgment be denied; and

(3) Defendants' motion for summary judgment be granted.

s/ Raymond J. Durkin
Raymond J. Durkin,
United States, Magistrate

Dated: December 22, 1986

Appendix F

IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF PENNSYLVANIA

CIVIL ACTION NO. 86-0083

TRI-BIO LABORATORIES, INC.,

Plaintiff

v.

UNITED STATES OF AMERICA, ET AL.,

Defendants

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NOTICE

Appendix F

NOTICE IS HEREBY GIVEN that the undersigned has entered the following: Report dated December 22, 1986, recommending that:

(1) Plaintiff's amendment of the complaint be permitted;

(2) Plaintiff's motion for partial summary judgment be denied; and

(3) Defendants' motion for summary judgment be granted.

Any party may obtain a review of the magistrate's above proposed determination pursuant to Rule 904.2, M.D. Pa., which provides:

> 904.2 Review of Case-Dispositive Motions and Prisoner Litigation—28 U.S.C. § 636(b)(1)(B).
>
> Any party may object to a magistrate's proposed findings, recommendations, or report, under subsections 901.4, .5, and .6 of these rules, *supra,* within ten (10) days after being served with a copy thereof. Such party shall file with the Clerk of Court, and serve on the magistrate and all parties, written objections which shall specifically identify the portions of the proposed findings, recommendations or report to which objection is made and the basis for such objections. The briefing requirements set forth in Rule 904.1 shall apply. A judge shall make a *de novo* determination of those portions of the report or specified proposed findings or recommendations to which objection is made and may accept, reject, or

modify, in whole or in part, the findings or recommendations made by the magistrate. The judge, however, need conduct a new hearing only in his discretion or where required by law, and may consider the record developed before the magistrate, making his own determination on the basis of that record. The judge may also receive further evidence, recall witnesses, or recommit the matter to the magistrate with instructions.

s/ Raymond J. Durkin
Raymond J. Durkin
United Statess Magistrate

Dated: December 22, 1986

APPENDIX G — RELEVANT STATUTES AND REGULATIONS

§ 360b. New animal drugs—Unsafe new animal drugs and animal feed containing such drugs; conditions of safety; exemption of drugs for research.

(a)(1) A new animal drug shall, with respect to any particular use or intended use of such drug, be deemed unsafe for the purposes of section 351(a) (5) and section 342(a) (2) (D) of this title unless—

> (A) there is in effect an approval of an application filed pursuant to subsection (b) of this section with respect to such use or intended use of such drug,
>
> (B) such drug, its labeling, and such use conform to such approved application, and
>
> (C) in the case of a new animal drug subject to subsection (n) of this section and not exempted therefrom by regulations it is from a batch with respect to which a certificate or release issued pursuant to subsection (n) is in effect with respect to such drug.

A new animal drug shall also be deemed unsafe for such purposes in the event of removal from the establishment of a manufacturer, packer, or distributor of such drug for use in the manufacture of animal feed in any State unless at the time of such removal such manufacturer, packer, or distributor has an unrevoked written statement from the consignee of such drug, or notice from the Secretary, to the effect that, with respect to the use of such drug in animal feed, such consignee—

(i) is the holder of an approved application under subsection (m) of this section; or

(ii) will, if the consignee is not a user of the drug, ship such drug only to a holder of an approved application under subsection (m) of this section.

(2) An animal feed bearing or containing a new animal drug shall, with respect to any particular use or intended use of such animal fee, be deemed unsafe for the purposes of section 351(a) (6) of this title unless—

(A) there is in effect an approval of an application filed pursuant to subsection (b) of this section with respect to such drug, as used in such animal feed,

(B) there is in effect an approval of an application pursuant to subsection (m) (1) of this section with resepect to such animal feed, and

(C) such animal feed, its labeling, and such use conform to the conditions and indications of use published pursuant to subsection (i) of this section and to the application with respect thereto approved under subsection (m) of this section.

(3) A new animal drug or an animal feed bearing or containing a new animal drug shall not be deemed unsafe for the purposes of section 351(a) (5) or (6) of this title if such article is for investigational use and conforms to the terms of an exemption in effect with respect thereto under subsection (j) of this section.

Appendix G

Filing application for uses of new animal drug; contents

(b) Any person may file with the Secretary an application with respect to any intended use or uses of a new animal drug. Such person shall submit to the Secretary as a part of the application (1) full reports of investigations which have been made to show whether or not such drug is safe and effective for use; (2) a full list of the articles used as components of such drug; (3) a full statement of the composition of such drug; (4) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing and packing of such drug; (5) such samples of such drug and of the articles used as components thereof, of any; animal feed for use in or on which such drug is intended, and of the edible portions or products (before or after slaughter) of animals to which such drug (directly or in or on animal feed) is intended to be administered, as the Secretary may require; (6) specimens of the labeling proposed to be used for such drug, or in case such drug is intended for use in animal feed, proposed labeling appropriate for such use, and specimens of the labeling for the drug to be manufactured, packed, or distributed by the applicant; (7) a description of practicable methods for determining the quantity, if any, of such drug in or on food, and any substance formed in or on food, because of its use; and (8) the proposed tolerance or withdrawal period or other use restrictions for such drug if any tolerance or withdrawal period or other use restrictions are required in order to assure that the proposed use of such drug will be safe.

Period for approval of application; period for, notice, and expedition of hearing; period for issuance of order

(c) Within one hundred and eighty days after the filing of an application pursuant to subsection (b) of this section, or such

additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either (1) issue an order approving the application if he then finds that none of the grounds for denying approval specified in subsection (d) of this section applies, or (2) give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) of this section on the question whether such application is approvable. If the applicant elects to accept the opportunity for a hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

Grounds for refusing application; approval of application; factors; "substantial evidence" defined

(d) (1) If the Secretary finds, after due notice to the applicant in accordance with subsection (c) of this section and giving him an opportunity for a hearing, in accordance with said subsection, that—

> (A) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b) of this section, do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof;
>
> (B) the results of such tests show that such drug is unsafe for use under such conditions or

do not show that such drug is safe for use under such conditions;

(C) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity;

(D) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions;

(E) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof.

(F) upon the basis of the information submitted to him as part of the application or any other information before him with respect to such drug, the tolerance limitation proposed, if any, exceeds that reasonably required to accomplish the physical or other technical effect for which the drug is intended;

(G) based on a fair evaluation of all material

facts, such labeling is false or misleading in any particular; or

(H) such drug induces cancer when ingested by man or animal or, after tests which are appropriate for the evaluation of the safety of such drug, induces cancer in man or animal, except that the foregoing provisions of this subparagraph shall not apply with respect to such drug if the Secretary finds that, under the conditions of use specified in proposed labeling and reasonably certain to be followed in practice (i) such drug will not adversely affect the animals for which it is intended, and (ii) no residue of such drug will be found (by methods of examination prescribed or approved by the Secretary by regulations, which regulations shall not be subject to subsections (c), (d), and (h) of this section), in any edible portion of such animals after slaughter or in any food yielded by or derived from the living animals;

he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that subparagraphs (A) through (H) do not apply, he shall issue an order approving the application.

(2) In determining whether such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof, the Secretary shall consider, among other relevant factors, (A) the probable consumption of such drug and of any substance formed in or on food because of the use of such drug, (B) the cumulative effect on man or animal of such drug, taking into account any chemically or pharmacologically

related substance, (C) safety factors which in the opinion of experts, qualified by scientific training and experience to evaluate the safety of such drugs, are appropriate for the use of animal experimentation data, and (D) whether the conditions of use prescribed, recommended, or suggested in the proposed labeling are reasonably certain to be followed in practice. Any order issued under this subsection refusing to approve an application shall state the findings upon which it is based.

(3) As used in this subsection and subsection (e) of this section, the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including field investigation, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and reasonably be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

Withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to health of man or animals

(e) (1) The Secretary shall, after due notice and opportunity for hearing to the applicant, issue an order withdrawing approval of an application filed pursuant to subsection (b) of this section with respect to any new animal drug if the Secretary finds—

> (A) that experience or scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved;

(B) that new evidence not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved or that subparagraph (H) of paragraph (1) of subsection (d) of this section applies to such drug;

(C) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that such drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof;

(D) that the application contains any untrue statement of a material fact; or

(E) that the applicant has made any changes from the standpoint of safety or effectiveness beyond the variations provided for in the application unless he has supplemented the application by filing with the Secretary adequate information respecting all such changes and unless there is in effect an approval of the supplemental application. The supplemental application shall be

treated in the same manner as the original application.

If the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the health of man or of the animals for which such drug is intended, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this sentence to suspend the approval of an application shall not be delegated.

(2) The Secretary may also, after due notice and opportunity for hearing to the applicant, issue an order withdrawing the approval of an application with respect to any new animal drug under this section if the Secretary finds—

(A) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports in accordance with a regulation or order under subsection (1) of this section, or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection;

(B) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve

its identity, strength, quality and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or

(C) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of.

(3) Any order under this subsection shall state the findings upon which it is based.

Revocation of order refusing, withdrawing or suspending approval of application

(f) Whenever the Secretary finds that the facts so require, he shall revoke any previous order under subsection (d), (e), or (m) of this section refusing, withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

Service of orders

(g) Orders of the Secretary issued under this section (other than orders issuing, amending, or repealing regulations) shall be served (1) in person by any officer or employee of the department designated by the Secretary or (2) by mailing the order by registered

mail or by certified mail addressed to the applicant or respondent at his last known address in the records of the Secretary.

Appeal from order

(h) An appeal may be taken by the applicant from an order of the Secretary refusing or withdrawing approval of an application filed under subsection (b) or (m) of this section. The provisions of subsection (h) of section 355 of this title shall govern any such appeal.

Publication in Federal Register; effective date and revocation or suspension of regulation

(i) When a new animal drug application filed pursuant to subsection (b) of this section is approved, the Secretary shall by notice, which upon publication shall be effective as a regulation, publish in the Federal Register the name and address of the applicant and the conditions and indications of use of the new animal drug covered by such application, including any tolerance and withdrawal period or other use restrictions and, if such new animal drug is intended for use in animal feed, appropriate purposes and conditions of use (including special labeling requirements) applicable to any animal feed for use in which such drug is approved, and such other information, upon the basis of which such application was approved, as the Secretary deems necessary to assure the safe and effective use of such drug. Upon withdrawal of approval of such new animal drug application or upon its suspension, the Secretary shall forthwith revoke or suspend, as the case may be, the regulation published pursuant to this subsection (i) insofar as it is based on the approval of such application.

Appendix G

Exemption of drugs for research; discretionary and mandatory conditions

(j) To the extent consistent with the public health, the Secretary shall promulgate regulations for exempting from the operation of this section new animal drugs, and animal feeds bearing or containing new animal drugs, intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of animal drugs. Such regulations may, in the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such article, of data (including but not limited to analytical reports by investigators) obtained as a result of such investigational use of such article, as the Secretary finds will enable him to evaluate the safety and effectiveness of such article in the event of the filing of an application pursuant to this section. Such regulations, among other things, shall set forth the conditions (if any) upon which animals treated with such articles, and any products of such animals (before or after slaughter), may be marketed for food use.

Food containing new animal drug considered unadulterated while approval of application for such drug is effective

(k) While approval of an application for a new animal drug is effective, a food shall not, by reason of bearing or containing such drug or any substance formed in or on the food because of its use in accordance with such application (including the conditions and indications of use prescribed pursuant to subsection (i) of this section), be considered adulterated within the meaning

of clause (1) of section 342(a) of this title.

Records and reports; required information; regulations and orders; examination of data; access to records

(l) (1) In the case of any new animal drug for which an approval of an application filed pursuant to subsection (b) of this section is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to experience and other data or information, received or otherwise obtained by such applicant with respect to such drug, or with respect to animal feeds bearing or containing such drug, as the Secretary may be general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination whether there is or may be ground for invoking subsection (e) or subsection (m) (4) of this section. Such regulation or order shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulation or order is applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this subsection to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

Filing application for uses of animal feed containing new animal drug; contents

(m) (1) Any person may file with the Secretary an application

with respect to any intended use or uses of an animal feed bearing or containing a new animal drug. Such person shall submit to the Secretary as part of the application (A) a full statement of the composition of such animal feed, (B) an identification of the regulation or regulations (relating to the new animal drug or drugs to be used in such feed), published pursuant to subsection (i) of this section, on which he relies as a basis for approval of his application with respect to the use of such drug in such feed, (C) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such animal feed, (D) specimens of the labeling proposed to be used for such animal feed, and (E) if so requested by the Secretary, samples of such animal feed or components thereof.

Same; period for approval of application; period for, notice, and expedition of hearing; period for issuance of order

(2) Within ninety days after the filing of an application pursuant to paragraph (1) of this subsection, or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either (A) issue an order approving the application if he then finds that none of the grounds for denying approval specified in paragraph (3) applies, or (B) give the applicant notice of an opportunity for a hearing before the Secretary under paragraph (3) on the question whether such application is approvable. The procedure governing such a hearing shall be the procedure set forth in the last two sentences of subsection (c) of this section.

Same; grounds for refusing application; approval of application; approval effective during existence of subsection (i) regulation

(3) If the Secretary, after due notice to the applicant in

accordance with paragraph (2) and giving him an opportunity for a hearing in accordance with such paragraph, finds, on the basis of information submitted to him as part of the application or on the basis of any other information before him—

> (A) that there is not in effect a regulation under subsection (i) of this section (identified in such application) on the basis of which such application may be approved;
>
> (B) that such animal feed (including the proposed use of any new animal drug therein or thereon) does not conform to an applicable regulation published pursuant to subsection (i) of this section referred to in the application, or that the purposes and conditions or indications of use prescribed, recommended, or suggested in the labeling of such feed do not conform to the applicable purposes and conditions or indications of use (including warnings) published pursuant to subsection (i) of this section or such labeling omits or fails to conform to other applicable information published pursuant to subsection (i) of this section;
>
> (C) that the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such animal feed are inadequate to preserve the identity, strength, quality, and purity of the new animal drug therein; or
>
> (D) that, based on a fair evaluation of all material facts, such labeling is false or misleading in any particular;

he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that subparagraphs (A) through (D) do not apply, he shall issue an order approving the application. An order under this subsection approving an application with respect to an animal feed bearing or containing a new animal drug shall be effective only while there is in effect a regulation pursuant to subsection (i) of this section, on the basis of which such application (or a supplement thereto) was approved, relating to the use of such drug in or on such feed.

Same; withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to health of man or animals

(4)(A) The Secretary shall, after due notice and opportunity for hearing to the applicant, issue an order withdrawing approval of an application with respect to any animal feed under this subsection if the Secretary finds—

> (i) that the application contains any untrue statement of a material fact; or
>
> (ii) that the applicant has made any changes from the standpoint of safety or effectiveness beyond the variations provided for in the application unless he has supplemented the application by filing with the Secretary adequate information respecting all such changes and unless there is in effect an approval of the supplemental application. The supplemental application shall be treated in the same manner as the original application.

If the Secretary (or in his absence the officer acting as Secretary)

finds that there is an imminent hazard to the health of man or of the animals for which such animal feed is intended, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this sentence shall not be delegated.

(B) The Secretary may also, after due notice and opportunity for hearing to the applicant, issue an order withdrawing the approval of an application with respect to any animal feed under this subsection if the Secretary finds—

> (i) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports in accordance with a regulation or order under paragraph (5) (A) of this subsection, or the applicant has refused to permit access to, or copying or verification of, such records as required by subparagraph (B) of such paragraph.
>
> (ii) that on the basis of new information before him, evaluated together with the evidence before him when such application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such animal feed are inadequate to assure and preserve the identity, strength, quality, and purity of the new animal drug therein, and were not made adequate within a reasonable time after receipt of written notice from the Secretary, specifying the matter complained of; or

(iii) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such animal feed, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of.

(C) Any order under paragraph (4) of this subsection shall state the findings upon which it is based.

Same: records and reports; regulations and orders; access to records

(5) In the case of any animal feed for which an approval of an application filed pursuant to this subsection is in effect—

(A) the applicant shall establish and maintain such records, and make such reports to the Secretary, or (at the option of the Secretary) to the appropriate person or persons holding an approved application filed under subsection (b) of this section, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) of this section or paragraph (4) of this subsection.

(B) every person required under this subsection to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

Certification of new drugs containing penicillin, streptomycin, chlortetracycline, chloramphenicol, or bacitracin; release prior to certification

(n) (1) The Secretary, pursuant to regulations promulgated by him, shall provide for the certification of batches of a new animal drug composed wholly or partly of any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, or bacitracin, or any derivative thereof. A batch of any such drug shall be certified if an approval of an application filed pursuant to subsection (b) of this section is effective with respect to such drug and such drug has the characteristics of identity and such batch has the characteristics of strength, quality, and purity upon the basis of which the application was approved, but shall not otherwise be certified. Prior to the effective date of such regulations the Secretary, in lieu of certification, shall issue a release for any batch which, in his judgment, may be released without risk as to the safety and efficacy of its use. Such release shall prescribe the date of its expiration and other conditions under which it shall cease to be effective as to such batch and as to portions thereof.

Same; provisions of regulations

(2) Regulations providing for such certifications shall contain such provisions as are necessary to carry out the purpose of this subsection, including provisions prescribing—

(A) tests and methods of assay to determine compliance with applicable standards of identity and of strength, quality, and purity;

(B) effective periods for certificates, and other conditions under which they shall cease to be effective as to certified batches and as to portions thereof;

(C) administration and procedure; and

(D) such fees, specified in such regulations, as are necessary to provide, equip, and maintain an adequate certification service.

Such regulations shall prescribe only such tests and methods of assay as will provide for certification or rejection within the shortest time consistent with the purposes of this subsection.

Same; exemption of drugs from subsection (n) requirements; applicability of section 357(c) of this title

(3) Whenever, in the judgment of the Secretary, the requirements of this subsection with respect to any drug or class of drugs are not necessary to insure that such drug conforms to the standards of identity, strength, quality, and purity applicable thereto under paragraph (1) of this subsection, the Secretary shall promulgate regulations exempting such drug or class of drugs from such requirements. The provisions of subsection (c) of section 357 of this title (other than the first sentence thereof) shall apply under this paragraph.

Appendix G

Name; exemption of drugs stored, processed, and labeled at other than manufacturing establishments or used in manufacture of other drugs

(4) The Secretary shall promulgate regulations exempting from any requirement of this subsection—

> (A) drugs which are to be stored, processed, labeled, or repacked at establishments other than those where manufactured, on condition that such drugs comply with all such requirements upon removal from such establishments; and
>
> (B) drugs which conform to applicable standards of identity, strength, quality, and purity prescribed pursuant to this subsection and are intended for use in manufacturing other drugs.

Same; procedure for issuance, amendment, or repeal of regulations

(5) On petition of any interested person for the issuance, amendment, or repeal of any regulation contemplated by this subsection, the procedure shall be in accordance with subsection (f) of section 357 of this title.

Same; determination of compliance with sections 351(b) and 352(g) of this title

(6) Where any drug is subject to this subsection and not exempted therefrom by regulations, the compliance of such drug with sections 351(b) and 352(g) of this title shall be determined by the application of the standards of strength, quality, and purity applicable under paragraph (1) of this subsection, the tests and

methods of assay applicable under provisions of regulations referred to in paragraph (2) (A) of this subsection, and the requirements of packaging and labeling on the basis of which the application with respect to such drug filed under subsection (b) of this section was approved.

June 25, 1938, c. 675, § 512, as added July 13, 1968, Pub.L. 90-399, § 360(b), 82 Stat. 343.

21 U.S.C. § 321.

Definitions; generally

For the purposes of this chapter—

> . . .(w) The Term "new animal drug" means any drug intended for use by animals other than man, including any drug intended for use in animal feed but not including such animal fees,—
>
> (1) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of animal drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof; except that such a drug not so recognized shall not be deemed to be a "new animal drug" if at any time prior to June 25, 1938, it was subject to the Food and Drug Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or

(2) the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions; or

(3) which drug is composed wholly or partly of any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, or bacitracin, or any derivative thereof, except when there is in effect a published order of the Secretary declaring such drug not to be a new animal drug on the grounds that (A) the requirement of certification of batches or such drug, as provided for in section 360b(n) of this title, is not necessary to insure that the objectives specified in paragraph (3) thereof are achieved and (B) that neither subparagraph (1) nor (2) of this paragraph (w) applies to such drug.

21 C.F.R. § 514.1 (1987)

SUBPART A — GENERAL PROVISIONS

Section 514.1 Applications.

(a) Applications to be filed under Section 512(b) of the Act shall be submitted in the form described in paragraph (b) of this section. If any part of the application is in a foreign language, an accurate and complete English translation shall be appended to such part. Translations of literature printed in

a foreign language shall be accompanied by copies of the original publication. The application must be signed by the applicant or by an authorized attorney, agent, or official. If the applicant or such authorized representative does not reside or have a place of business within the United States, the application must also furnish the name and post office address of, and must be countersigned by, an authorized attorney, agent, or official residing or maintaining a place of business within the United States. Pertinent information may be incorporated in, and will be considered as part of an application on the basis of specific reference to such information, including information submitted under the provisions of Section 511.1 of this chapter, in the files of the Food and Drug Administration; however, the reference must be specific in identifying the information. Any reference to information furnished by a person other than the applicant may not be considered unless its use is authorized in a written statement signed by the person who submitted it.